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OCCASIONAL LECTURE.

Suppurative Diseases of the Lung: Report on a Series of Bronchoscopic Observations.[1]

By Chevalier Jackson, M.D., Sc.D., LL.D.

The subject of pulmonary suppuration is so large, and its literature so voluminous, that any practical presentation of it must be limited in some way. On the present occasion this is fortunate, because, as I have before stated, the bronchoscopist sees things narrowly through a small tube, metaphorically as well as actually. However, clinical facts are always worthy of record, and if the accompanying deductions should be deemed erroneous, the clinical facts, at least, will be available for consideration. The data presented under each heading are collected from notes of cases at the bronchoscopic clinic; no attempt is made comprehensively to review each subject, or completely to present each case; such an attempt would so increase its bulk as to defeat all efforts to make the presentation practical.

Aid of bronchoscopy to the physician.—When, and in what kind of case of pulmonary suppuration, the bronchoscopist may be of aid to the medical attendant or the internist, is a difficult question to answer except in case of foreign body. To begin with, it is rarely possible to be certain that any case of pulmonary suppuration is not one of foreign body, and in many cases the only way to determine whether or not a foreign body is present is to look into the suppurating focus with the bronchoscope. All of the internists with whom we have worked call frequently for the aid of the bronchoscopist in diagnosis and treatment of suppurative diseases of the chest; but it would be difficult to present a categoric list of the different conditions in which this aid is requested. Perhaps the largest number of cases could be classified under the general heading of bronchial obstruction. In diagnosis, when the physical signs and the Roentgen-ray examination indicate that there is a diminished amount of air entering a certain portion of a lung, the outstanding problem is to determine what is the cause of the obstruction. Sometimes the causes can be determined by the Roentgen-ray examination, but in other cases the only way to determine the character of the obstruction is to put down a bronchoscope and examine the lumen of the obstructed bronchus. In many cases the internist calls upon us to supply him with a specimen of pus taken from the focus in the lung uncontaminated by the mouth or the stagnant secretions that accumulate above the focus, which are not always representative of the purulent process in the suppurative focus itself. In these cases we aspirate a gross quantity of pus, and then, in a separate small collector, get a few drops of pus directly from the focus (fig. 1); it is often deep down in the lung, sometimes up around the corner in an ascending

[1] At a Meeting of the Society held October 14, 1930.

branch of the upper lobe bronchus. These special collections are for laboratory study and the preparation of vaccines. Sputum contains not only contaminations from the mouth, but also pus that has been stagnant in the bronchi for weeks and sometimes for months. During this period of stagnation a constant battle has been going on among the various bacterial organisms which are constantly invading with the inspired air. In the warm, moist incubating chamber of the tracheo-bronchial tree, with an abundance of pabulum, the mixed infections run riot and render the determination of the primary infective agent impossible. It is here that the bronchoscopist, with his tiny 5 or 4 mm. tube, clears the way down to the very depths of the tracheo-bronchial tree, and, inserting a still finer aspirating tube into the little fistula or small branch bronchus from which the pus is coming, is able to obtain a sample that will show the primary or the most important organism. This infective agent is usually not to be found predominating among the swarms of bacteria of every kind present in sputum.

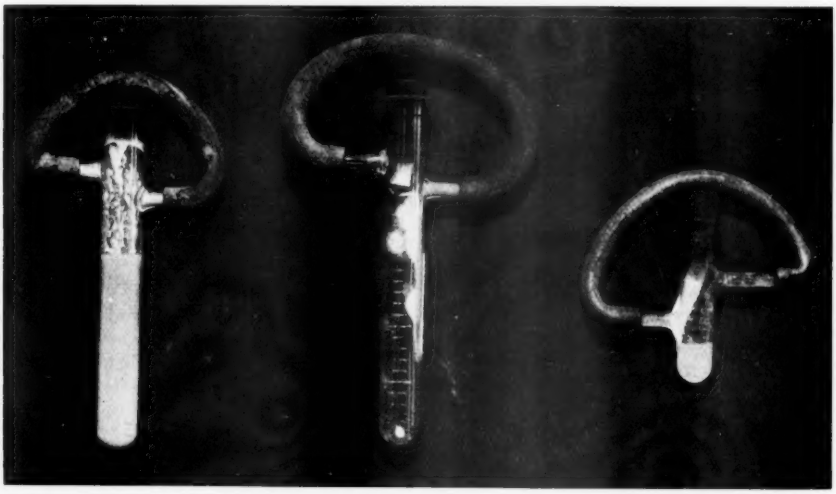

FIG. 1.—When a large quantity of pus is present, as shown by the collecting tube at the left, it is better first to aspirate the larger bronchi; then with a small collector or collectors to get one or more specimens of the pus from small bronchi, fistulæ, or whatever may seem to be the important focus. The collecting tube in the centre shows pus so thick and viscid that it will not run down the wall of the tube. This kind of pus is one of the chief factors in the perpetuation of suppurative diseases of the lungs; it favours stagnation by clogging the cilia and resisting tussive expulsion.

In most cases of suppurative diseases of the lung medical care and management are sufficient to bring about recovery; in certain other cases these means are sufficient to prevent the patient from getting any worse, but he does not improve. In this latter class of case it frequently happens that the addition of bronchoscopic aspiration—in other words, peroral drainage—is sufficient to turn the tide in favour of recovery. This turning of the tide has occurred in so many cases, and in the hands of so many different bronchoscopists, as to rule out the possibility of mere coincidence. A few examples of this kind are given in the cases herein reported; in hundreds of other cases the details have been given in the published reports of the bronchoscopic clinics of Philadelphia and elsewhere.

Summarizing the matter of the indications for bronchoscopy as an aid to the medical attendant, it may be stated that in our daily work we depend largely upon the decision of the internists with whom we work. The medical attendant and the internist have a breadth of view that no specialist can have. The internists with whom we work call upon us to do a bronchoscopy whenever they feel that a specular examination is needed. The bronchoscope is a bronchial speculum. It differs from other specula in that it requires a special technique for safety and utmost usefulness.

ÆTIOLOGY.

The prime ætiological factor is of course infection. There are many sources of infection, but the most important seem to be the teeth, the tonsils and the nasal accessory sinuses. Oral sepsis is a large factor, since, as shown by bronchoscopic observations, every human being inspires secretions from the pharynx into the trachea during sleep. The cough reflex, which is the watch-dog of the lungs, promptly drives out the secretions, and with them most of the invading host. This is the first line of defence. The few that remain are wafted out along with the secretions by the cilia, the second line of defence; or they are destroyed by the cells and juices; these are the third and fourth lines of defence. As shown by bronchoscopically removed specimens, air-borne infective organisms become fewer and fewer from above downward. In health the very small bronchi are usually sterile.

Though the prime ætiological factor in suppurative disease of the lung is infection, for the infective agents to get a foothold, additional ætiological factors are required, and on some of these certain bronchoscopic observations seem to have a bearing. The ætiological factors on which we have data in the records of cases, other than those of foreign body, are as follows: 1, Inefficiency of the cough reflex; 2, opiates and other drugs; 3, bronchial obstruction; 4, inflammatory stenosis; 5, obstructive atelectasis; 6, benign growths; 7, malignant growths; 8, nasal accessory sinus disease; 9, tuberculosis; 10, syphilis; 11, Vincent's infection; 12, spirochætosis; 13, actinomycosis; 15, adenopathy and anthracosis; 16, asthma; 17, pneumonia; 18, operations.

Inefficiency of the cough reflex.—Many patients without suppurative disease cough violently, and many almost incessantly. We are often called upon to make a diagnostic bronchoscopic examination to determine the cause of the cough in such cases. In strong contrast with this, we are never asked to determine why the patient does not cough. Yet we have seen a very large number of cases of inefficiency of the cough reflex and quite a number in which the patient was drowning in his own secretions because the cough reflex was totally abolished [4, 18]. In lesser degree than this, it is quite usual to see a mild and indifferent coughing effort in a patient who could do better in the way of getting up pus if he would cough hard enough.

I have repeatedly referred to the bronchoscopic evidence of the fact that in all cases of chronic suppurative disease of the lungs the cough reflex is more or less inefficient. After the patient has coughed and coughed for perhaps hours, and has brought up all the sputum he can, bronchoscopic examination will reveal pools of pus that he has been unable to remove, stagnant pus that has been there for days or weeks, as shown by the fact that it is decomposed by saprophytes and sometimes discoloured by chromogenic bacteria. This pathologic inefficiency of the cough reflex is often increased by the ill-advised administration of morphine, codeine and other antibechics.

The inefficiency of the cough reflex is noted by Mr. R. Graham Brown in a paper read before a Section of this Society.[1] He states: "A good plan with these

[1] *Proceedings*, 1928, xxi, 69 (Sect. Laryng. 69).

children is to hold them upside down and then make them cough. Upon the appearance of thick sputum most parents have expressed great surprise and have assured me that they have never previously seen any similar sputum from the child."

Drugs.—Certain drugs, especially opium derivatives and atropine, probably lower the efficiency of the cough reflex. The ill-advised use of opiates, by paralysing the cough reflex, as I have often said "drugging the watchdog to sleep," on theoretic grounds would seem to be an ætiological factor by decreasing the efficiency of spontaneous drainage, and retaining in the warm, moist, bronchial incubating chamber the pyogenic and saprophytic organisms. Atropine renders the secretions thicker and more tenacious, hence more difficult to expel. It does not diminish pus formation, but it diminishes the secretions that ordinarily dilute the pus and lubricate it for expulsion.

Bronchial obstruction.—Bronchoscopic observations indicate that one of the most important ætiological factors in suppurative diseases of the lung is bronchial obstruction. While it is true that bronchial obstruction has in a general way been regarded as a factor in the ætiology of pulmonary diseases, its full importance was not realized; nor was it possible to determine the extent to which this factor was concerned in any particular case, prior to the development of bronchoscopy.

It is an established fact that bacterial infection is the primary factor in suppurative diseases of the lung, but bronchoscopy has demonstrated that infective agents have great difficulty in obtaining a foothold against the defensive powers of the lung while these are unimpaired. It is well known that all the cells and juices in the body possess defensive powers; otherwise the human race would long ago have been exterminated. In addition to those defensive powers, the lungs have special means of defence, namely the cilia and the cough reflex. For the greatest effectiveness of these two special defensive mechanisms it is necessary that ventilation and drainage be unimpaired; slight bronchial obstruction will impair their efficiency, and complete bronchial obstruction will annihilate them.

When one thinks of bronchial obstruction it is natural to infer that a bronchus may be partially or completely obstructed; and that these two types are quite common is shown by post-mortem examinations; but only in the living can it be demonstrated (by bronchoscopic and Roentgen ray studies) that there exists a third type of obstruction, in which there is an action like a check-valve. In mechanics a check-valve is one that permits a flow in one direction only, the direction being determined by the construction or, rather, the placing of the valve. Check-valves are fundamental to pumps. Any gas or any fluid may be pumped into or out of a reservoir by the same pump, according to which way the check-valve is set. In the tracheo-bronchial tree the check-valve may be set against the ingress or egress of air [42].

All three types of bronchial obstruction may be produced by (1) tissues, (2) foreign bodies, and (3) secretions acting as foreign bodies [3].

Obstructive atelectasis as a cause of suppuration.—Notwithstanding the fact that therapeutic pneumothorax is regarded as a very efficient method of treating some forms of pulmonary suppuration, bronchoscopic observations have shown that in hundreds of cases atelectasis is a cause of suppuration. This refers, however, only to obstructive atelectasis, a condition due to a valvular mechanism, as elsewhere herein explained. The lung will not long remain collapsed as the result of obstruction without suppuration following. This suppuration at first takes the form of drowned lung, in which the normal passages are filled with pus. If this condition persists for any length of time the walls of the natural passages break down and abscess is the result. Our experience leads us to believe that many of the cases thought to be post-operative pneumonia followed by abscess are really

atelectasis followed by abscess. A number of patients known to have had post-operative atelectasis have been referred to us with well-developed abscesses, such patients being referred for bronchoscopic aspirations.

The clinical experience at the bronchoscopic clinics of Philadelphia seems to justify the conclusion that theoretic decisions as to the pathologic mechanism of post-operative atelectasis must be considered ill-founded if neither bronchoscopy nor necropsy has been done—and even necropsy may lead to erroneous deductions. We have uncorked so many bronchi, thus permitting the tributary lung or lobe to expand, that perhaps we may be somewhat too sceptical as to other ætiological mechanisms. We have seen bronchoscopically over one hundred cases, and in every one of them there were evidences of bronchial obstruction. In a few cases there was a pre-existing compression stenosis from organic disease; in one case there was an endo-bronchial benign growth (œdematous polyp) of unknown duration, in another case there was an early carcinoma.

Obstructive emphysema is a cause of suppuration, but not so promptly or so frequently as obstructive atelectasis. Considering the fact that in obstructive emphysema we have obstruction to drainage combined with hyper-aëration, the slower development of suppuration seems to indicate that aëration is a greater defensive power than drainage. In fact, in the presence of emphysema due to foreign body or disease not of itself provocative of suppuration, there is for a long time very little tendency to formation of pus. It is well to remember that obstructive emphysema is usually followed, sooner or later, by obstructive atelectasis; then suppuration rapidly supervenes.

Inflammatory stenosis.—Bronchoscopic observations have convinced me that an inflammatory narrowing or closure of a bronchus is one of the most important causes of pulmonary abscess and other suppurative diseases of the lung. In a sense it must be called a secondary factor, inasmuch as there must be an inflammatory process preceding it in order that there may develop an inflammatory stenosis of the bronchus. Nevertheless, if my deductions are correct, the defensive powers of the lung could readily repel the invaders if it were not for the interference with drainage and ventilation caused by the stenotic encroachment upon the lumen by the swelling of the bronchial mucosa. Moreover, if the swelling persists for any length of time, it becomes a permanent condition because of the building up of a ring of inflammatory new formation. After this new formation becomes fibrous, and cicatricial contraction sets in, we have a steadily increasing stenosis. This is well illustrated in the following case.

Case I.—A woman, aged 18, was referred for diagnostic bronchoscopy from a surgical clinic. The symptoms were spasmodic attacks of coughing with expectoration of about a cupful and a half of foul pus, pain in the chest, inability to take a deep breath without pain, fever in the afternoon. The cough and expectoration had been noticed intermittently for seven years, but during the six months prior to admission there had been great exacerbation of the symptoms and a weight loss of 12 lb. For a month the patient had been bedfast. Roentgen-ray examination revealed a dense triangular shadow in the right lower lobe, with obliteration of the outline of the diaphragm.

Bronchoscopic examinations revealed a complete stenosis of the lower lobe stem at a distance of about two centimetres below the orifice of the middle lobe bronchus. The bronchial mucosa, after the aspiration of a large quantity of foul pus, was found to be very inflammatory, thickened, red and velvety. At the site of the stenosis was an annular red obstruction, in the centre of which was a small bead of pus. There was no movement of the pus indicating either inflow or outflow of air. An aspirator was inserted and the pus withdrawn; it was blood-stained and foul. This material was separately collected for special bacteriological examination. The region below the stenosis could not be explored, because the lumen of the stricture was too small for the bronchoscope to enter. Dilatations were therefore commenced and were continued, along with bronchoscopic aspirations, for a period of three months. At the end of that time the stricture had been completely dilated and the

five-millimetre bronchoscope could be inserted. The cavity below was somewhat irregular in shape, and branched. It was lined with epithelium similar in colour to that of the bronchus. All of the symptoms had disappeared, and the patient was sent home fully recovered. A recent report, one and a half years after discharge, states that she remains in good health. Interesting points in connection with this case are the following: (1) The patient had had a productive cough for seven years. Quite suddenly, seven months prior to admission, there had been a great exacerbation in the cough, with chilliness and fever, especially in the afternoon. The cough, while productive at times of a very large quantity of foul sputum, was, in the interval, unproductive, indicating interrupted drainage. It seems logical to infer that though up to seven months previously the stenosis had not been so great as to interfere very seriously with drainage, yet it had been sufficient to prevent the infection being overcome by the defensive power of the lung. The exacerbation of the symptoms, along with the physical signs and the Roentgen-ray examinations, indicated the probability that seven months prior to admission the drainage and ventilation of the suppurative area had become completely blocked. (2) The surgeon, on receiving the report of the bronchoscopic examination showing a stenosis of the bronchus, advised bronchoscopic aspiration instead of thoracotomy, because of his belief that the stricture was a very important part of the perpetuation of the suppuration, and that its dilatation by bronchoscopic means was the primary indication. (3) No medication of any kind, either local or general, was used in the treatment of this patient. The good results were due solely to dilatation of the stricture and drainage of the pus. (4) The beginning of the improvement coincided precisely with the aspiration of the pus and the dilatation of the stricture; improvement was steadily progressive as enlargement of lumen and lessening of stagnation resulted from the bronchoscopic treatment. If this were an isolated case it might carry little weight, but it is simply an example of hundreds. (5) The secretion from this patient was so thick and tenacious that it would not run down in a collecting tube. This viscosity was a large factor in perpetuating the suppuration, and its frequent bronchoscopic removal doubtless contributed largely to the good results obtained by bronchoscopic dilatation of the stricture.

Foreign body.—This presentation is not concerned with foreign body, yet there have been so many cases of suppurative disease of the lungs due to overlooked foreign body that this ætiological factor should always be regarded as the first possibility to be excluded, and especially so because the suppuration will not cease until the foreign body is removed; furthermore, of all the kinds of pulmonary suppuration, that due to foreign body is the most quickly and satisfactorily cured. Every now and then a patient is sent to the clinic for bronchoscopic aspiration of a chronic abscess or bronchiectasis, and we find a foreign body, most often a bone or a tooth, because these substances are not sufficiently opaque to show through the associated pathological shadows in Roentgen-ray examinations. Many such cases were previously reported [41] and many more have since come to the clinic.

Endogenous foreign bodies producing bronchial obstruction.—We have had four cases of broncholith removed bronchoscopically. In all, suppuration was present. In one of the cases great improvement, in fact symptomatic cure, resulted from the bronchoscopic removal of the foreign body. In the other three cases the condition of the patient remained unimproved. In marked contrast to the relative rarity of broncholith we have had many cases of teeth and a few cases of fragments of human cartilage and bone. The commonest of all endogenous foreign bodies, however, are masses of secretions and fibrinous exudate. Bits of the patient's own cartilage or bone are also represented among the foreign bodies removed in our series of cases.

Fibrinous casts are relatively rare, but pus or mucoid secretion massively coagulated by an excess of fibrin is exceedingly common. The massively coagulated mucoid secretion is most often seen in asthmatic patients.

Benign growth as a cause of suppuration.—Though benign growths cannot be called common, we have encountered quite a number with the bronchoscope, and in most instances they had been altogether unsuspected by the clinicians, the roentgenologists or the bronchoscopists. The physical signs and the

Histologic structure of endo-bronchial tumour removed through the mouth by bronchoscopy. At the top is a low-power view showing a shell of bone (B) enclosing marrow cells (M) and surrounded by osteogenic cells (O). In the lower illustration is shown a higher magnification of a field taken from the neighbourhood of the dotted circle (F). At T and T are trabeculæ of bone radiating from the bony shell.

Photo-micrograph from a section of a bronchoscopically removed bony tumour that caused atelectasis of the lower lobe and at the same time emphysema of the upper lobe. Both of these phenomena, as well as the secondary suppuration, disappeared after the bronchoscopic removal of the growth. The basic attachment is fibrous, but the tumour has a central thin shell of normal bone containing normal bone-marrow. Surrounding the shell are granulation tissue and osteogenic cells through which run trabeculæ of bone. This structure distinguishes this rare tumour from the not uncommon calcified nodule.

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Roentgen-ray examination revealed the fact that there was bronchial obstruction of some one of the three types mentioned; but it remained for the diagnostic bronchoscopy to determine that the bronchial obstruction was due to a benign growth. The following case is an interesting example.

Case II.—Endobronchial bony tumour.—A man, aged 46, was referred for bronchoscopic examination because the consultants had questioned the medical diagnosis of bronchiectasis and the surgical diagnosis of interlobar empyema. The Bordet-Wassermann test had been repeatedly negative; the sputum and blood examinations and various laboratory studies had shown nothing of outstanding significance.

Symptoms.—The symptoms complained of were cough, expectoration of foul sputum, —about a cupful daily—pain in left side of chest, intermittent, and also on coughing; weight-loss, chilliness, fever (to 103° F.) and sweating.

Physical signs (Dr. Harold Robertson).—The signs were practically normal on the right side. On the left the breath sounds were diminished over both lobes, and the percussion note and vocal fremitus were diminished over the lower lobe.

Roentgen-ray examination (Dr. Willis F. Manges).—Fluoroscopy and roentgenograms gave evidence of obstructive emphysema of the left upper lobe and obstructive atelectasis of the left lower lobe, with evidence of a suppurative process in the left lower lobe (fig. 2).

Bronchoscopy.—Bronchoscopic examination (Tucker) revealed pus coming from the left lung. On aspirating this a pedunculated tumour-like mass was found obstructing the left upper and lower-lobe bronchi. The entire mass came away with little resistance in the grasp of tissue forceps.

Histology (Dr. E. A. Case).—This mass is partly covered with epithelium, and in part the surface covering is absent. The epithelium is of the stratified type, but in a very few small places it assumes squamous characteristics. In the centre of the mass there is a piece of bone about 5 mm. by 3 mm. It is elliptical in outline, and its centre is composed of very cellular tissue containing, in addition to lymphocytes, polymorphonuclear and mononuclear cells, others resembling those of bone-marrow, including giant-cells. About this bone the tissue is fibrous, ranging in density from very loose œdematous material to dense areas, suggesting cartilaginous development. Small masses of fatty tissue are present. Glands dip in from the surface epithelium. Where the surface epithelium is lost there is a covering of fibrin, with blood and leucocytes. *Diagnosis.*—It is hard to place the growth. I am of the opinion that it is primarily an inflammatory process with bone formation.

(Dr. Baxter L. Crawford).—"The tissue resembles the cross-section of bone with marrow development. It is not the type of osteogenic metaplasia seen in calcified nodules of the lung."

(Dr. James Ewing).—"The section of bronchial tumour shows a remarkable condition, which is a central shell of normal bone containing marrow. The bone shell is 4 mm. in diameter. It is surrounded by chronic productive new tissue, rather fibrous, with outrunning trabeculæ of bone. The epithelial layer is missing over most of the section, which is largely composed of granulation tissue. There is no sign of a malignant process in this tissue. I am at a loss to account for such a condition in the bronchus and I do not think I have seen it before." (*See* plate.)

Malignant growths as a cause of suppuration.—Malignant growths of the lung can cause suppuration in two ways, namely: (1) by obstruction to ventilation and drainage; (2) by ulceration and breaking down of tissue.

Local anæsthesia.—In quite a number of cases of post-tonsillectomy pulmonary abscess that have come to the bronchoscopic clinic the anæsthetic was cocaine used locally. The abolition of the cough reflex, the drugging asleep of the watch-dog of the lungs, undoubtedly permits the entrance of secretions and blood into the trachea and even the bronchi during operations; we have repeatedly seen this. We have also seen intense congestion of the tracheo-bronchial tree result. This would account for the obstructive atelectasis, and for the cases of abscess that have followed post-operative atelectasis in the patients whose operations were performed under local anæsthesia.

B

A

FIG. 2.—(A) Obstructive emphysema of the left upper lobe and obstructive atelectasis of the left lower lobe in a man aged 46, due to an endobronchial bony tumour. (B)—four months later—showing the restoration of normal function after bronchoscopic removal of the tumour.

General anæsthesia has long been recognized as a cause of pulmonary suppuration, though it is often impossible ætiologically to separate the anæsthesia from the results (embolism for instance) of the operation for which it was given. My personal opinion is that post-anæsthetic suppuration is not secondary to a pneumonia, as so often thought, but to an obstructive atelectasis the physical signs of which are mistaken for those of pneumonia. The bronchial obstruction I believe to be due to coagulated secretions in the bronchi. The cause of the massive coagulation of secretion I believe to be vascular congestion which has increased the amount of fibrinogen. These deductions are very largely supported by the clinical evidence at the bronchoscopic clinic, but of course we must recognize the fact that this evidence is of little value negatively; it cannot set aside autoptic evidence of a pneumonia following anæsthesia. Examining the clinical evidence we have made the following observations:—

(1) We have been called upon to examine bronchoscopically many patients with atelectasis following operations under ether, and in many of these cases a diagnosis of pneumonia had been made. Invariably we have found obstructive conditions causing an atelectasis when the patient was bronchoscopically examined within a few days of the operation. In other cases, in which bronchoscopy was postponed, we found a suppurative process evidently a sequel of an atelectasis.

(2) In many patients sent to the clinic with pulmonary abscess we have gone back over the record of the physical signs and Roentgen-ray examination from the onset of the post-anæsthetic illness and have found these records to fit a diagnosis of atelectasis better than one of pneumonia.

(3) Thick viscid secretions removed from a bronchus in "uncorking" an obstructive atelectasis have been examined by Dr. John Kolmer and found to contain a large excess of fibrin. It was Dr. Kolmer who suggested excess of fibrin as a cause of the massive coagulation of pus and secretions in the bronchi. As to the cause of the excess of fibrin the congestion of the bronchial mucosa incidental to ether anæsthesia would probably account for an excess of fibrinogen. This is inference, though the constant presence of mucosal congestion in general anæsthesia is a clinical fact many times observed in the early days when general anæsthesia was used for bronchoscopy, and occasionally observed since in cases in which we have been asked to insert a bronchoscope because of obstructive dyspnœa in a patient anæsthetized for a general surgical procedure.

Tonsillectomy and other operations about the upper air passages are causes of pulmonary suppuration. Bronchoscopy has afforded much evidence, none of it conclusive, on the ætiology of this kind of suppuration. This will be briefly considered later in connection with other phases of this interesting and important class of case.

Post-operative pneumonia.—From our experience in the bronchoscopic clinic it may be said that true lobar pneumonia, as the internist understands the term, is an exceedingly rare occurrence as a complication of any surgical procedure. Bronchoscopies done in cases clinically considered pneumonia have nearly always shown the condition to be obstructive atelectasis. When the obstruction is not removed those defensive powers of the lung that are dependent upon ventilation and drainage (the cilia and the cough-reflex) are annihilated; the few organisms always present in the bronchi multiply; drowned lung succeeds the atelectasis; and pulmonary abscess follows. Through all this sequence the outstanding physical sign is dullness on percussion. This, when not closely analysed in comparison with the auscultatory and other signs, supports a diagnosis of pneumonia, and when the signs and symptoms of pulmonary abscess supervene, the case is erroneously classed as a post-operative pneumonia followed by pulmonary abscess. Of course there are infective and infarctive types of bronchitis and pneumonitis following operations, and these are called post-operative pneumonia also. They are amenable to bronchoscopic aspiration and the sooner the aspirations are commenced the better the results.

Tuberculosis.—Bronchoscopy has some important relations to tuberculous suppurative disease of the lung. Some of these are: (1) Assisting in the diagnosis by removal of specimens of secretions from pulmonary foci; (2) aid in diagnosis of tuberculosis of the bronchial wall, glandular invasions of the bronchi and resulting cicatricial stricture; (3) improvement of drainage by dilatation of stenoses; (4) removal of obstructive pathologic tissues and materials.

The following cases are examples:—

Case III.—Tuberculosis of the bronchial wall.—Male, aged 32; seen in consultation with Dr. Louis H. Clerf. The symptoms were dyspnœa, increased on exertion; paroxysmal cough; very slight expectoration: wheezing heard at the open mouth; all dating from a "cold" three months before. Sputum and serological examinations were negative. Dr. Thomas McCrae found physical signs of bronchial obstruction on the left side and advised bronchoscopy. Dr. Willis F. Manges found Roentgen-ray signs of old obstruction by non-opaque tissue or other substance in the left bronchus, with air passing both in and out but in very much diminished amount. For determination of the character of the obstruction he advised bronchoscopy. At bronchoscopic examination the larynx, trachea, carina and right bronchus were normal, and the orifice of the left bronchus was apparently normal; but in the left bronchus at a point about 2 cm. beyond the carina there was an area of superficial erosions of the mucosa covered with greyish exudate, involving the median wall and extending along the anterior and posterior walls downward to the orifice of the left upper-lobe bronchus. This was partially occluded by small, flat, pale fungations. The mucosa of the lower-lobe bronchus was infiltrated, encroaching upon the lumen to the extent of obliteration on forced expiration and on coughing. The greater axis of the stenosed lumen was in the coronal plane. There was not much secretion, but sufficient was obtained from the surface of the lesion with the bronchoscopic aspirator to serve for laboratory study, including the inoculation of a guinea-pig, by Dr. C. J. Bucher. Tubercle bacilli were found in the bronchoscopically aspirated secretions, and the inoculated animal died seven weeks later from tuberculosis. This case shows the value of bronchoscopic examination in cases of unexplained cough, especially when there are signs of bronchial obstruction. Tuberculosis of peripheral bronchi is the usual accompaniment of pulmonary tuberculosis, but primary tuberculosis of the wall of either main bronchus with uninvolved pulmonary parenchyma is probably a very rare disease, so far as can be determined by necropsy reports; but in the approaching era, when it will be considered inadvisable to treat endobronchial symptoms without endobronchial examination, the statistics may require revision.

Case IV.—Tuberculosis of the left upper lobe diagnosed from a bronchoscopically removed specimen.—Woman, aged 19, had occasional cough and hæmoptysis. Steady increase in weight, and absence of confirmation by Roentgen-ray and sputum examinations, on the one hand, and on the other, proven neurotic and hysteric manifestations plus gingivitis led to the diagnosis of voluntary production of blood from the gums, and to the abandonment of a diagnosis of pulmonary tuberculosis. The patient was taken off the anti-tuberculous régime and was sent to college. The institutional physician asked for a bronchoscopic examination, chiefly to determine the source of the hæmoptysis. Bronchoscopy showed a streak of blood leading all the way downward from the posterior commissure to the left upper lobe bronchial orifice. A few beads of apparently mucopurulent secretion were found just within the orifice and were removed. The secretions removed bronchoscopically were found to contain tubercle bacilli, and guinea-pig inoculations were positive. The progress of the case showed it to be an intractable and ultimately fatal pulmonary tuberculosis. This case is an example of hundreds in which the source of the hæmoptysis was discovered by bronchoscopy. It is also an example of the large number of cases in which tubercle bacilli were found and positive guinea-pig tests obtained with bronchoscopically removed secretions, after a long series of negative results obtained from sputum.

Syphilis of the lung.—Lesions of the upper end of the trachea due to extensions of laryngeal syphilis are relatively common; progressively downward in the tracheobronchial tree these lesions become less and less common. Omitting the cases of laryngeal extension, I have gone over the records of eighty-eight cases of tracheobronchial syphilis encountered at the bronchoscopic clinic. The lesions were ulcers,

gummata, perichondritis, chondrial necrosis, cicatrices and compression stenoses; all were accompanied by bronchial obstruction; and all the three types of this were found:—by-pass, with a wheeze heard at the open mouth; check-valve, with obstructive emphysema or obstructive atelectasis; stop-valve, with atelectasis, drowned lung, abscess or bronchiectasis.

In most cases the diagnosis of syphilis of the lung is based upon the observation of a pulmonary lesion in a patient who has a positive serological test. This diagnosis is to be confirmed or doubted according to whether or not the patient responds to antisyphilitic treatment. In quite a number of cases that have either failed to improve or have improved but slightly under vigorous medication, we have been asked to make a bronchoscopic examination. In a series of forty-seven cases of this kind, some of which are included in the series of eighty-eight cases above mentioned, seventeen were found to have cancer; a number were found to have cicatricial stenosis which may have been due to a previous syphilitic lesion; in three there were compressive stenoses of the main bronchi (two left, one right) that were interfering with ventilation and drainage. It is probable that the stenoses were due to masses of glands in the mediastinum. Of the remaining cases seven had conditions suggestive of very extensive pulmonary changes due to prolonged syphilitic suppuration of the lung tissue, but they are not included in the series of eighty-eight proven cases above mentioned. A number of cases of gumma were encountered; the following is one of the most interesting:

Case V.—Gumma of the left bronchus.—Male, aged 42, had complained of cough, occasional fever, and the expectoration of pus for a number of months. Because of the knowledge of an initial lesion and a strongly positive serological test, the patient was given active antisyphilitic treatment. Under this medication the suppuration, as indicated by the amount of expectoration, did not diminish; nor did the shadow of a mass visible to the left of the median line, as shown in the roentgenogram, diminish in size. There gradually developed signs of bronchial obstruction on the right side. The breath sounds were very much diminished; the percussion note was impaired at times, at other times it was tympanitic. Roentgen-ray examination when the note was tympanitic showed that there was an obstructive emphysema of the right lung. On bronchoscopic examination I found a large rounded nodule covered with epithelium, but not showing any sign of bronchial rings, located in the right bronchus at the level of the orifice of the right upper lobe bronchus, but springing from the median wall. A specimen removed for examination was reported upon by Jonathan Wright as a gumma. As there was no stenosis of the left bronchus, the presumption was that the mass visible in the Roentgen-ray examination was a large gland. Under prolonged and more energetic treatment this mass diminished in size somewhat, but it never disappeared while the patient was under observation. At a bronchoscopy three months after removal of the specimen reported as a gumma, no trace of the lesion could be found. The bronchus seemed to be normal.

Vincent's infection.—This disease is probably more often associated with bronchial suppuration than is generally supposed. Whether or not the spirillum of Vincent and the fusiform bacillus are primary invaders is uncertain, but the experience at the bronchoscopic clinic points strongly to its being an active ætiological factor in the continuance of the suppuration. The almost constant presence of Vincent's organisms in the mouth renders positive findings in sputum examinations worthless; and the failure to find the organisms in sputum when we have found them swarming in the residual pus in the bronchi, indicates that negative reports on sputum are as unreliable as positive findings.

Case VI.—Vincent's infection of the bronchi.—Man, aged 29. Symptoms: cough with expectoration of foul greenish material amounting to about a cupful in twenty-four hours; severe hæmorrhage a few months before admission, and lesser hæmorrhages continuously; slight dyspnœa. History of choking on a glass-headed pin when 4 years of age. Nine years

prior to admission the patient had an automobile accident resulting in fractured ribs and other injuries; bed-fast for eight months; pain in left side of chest ever since. Different roentgenologists reported differently on the Roentgen-ray findings of the chest. One roentgenologist reported the shadow of a pin in the left lower lobe, surrounded by an area of shadows indicating chronic inflammation; another roentgenologist reported abscess but no pin; still another roentgenologist reported a shadow in the left upper lobe which he regarded as tuberculous. All the roentgenologists agreed that bronchoscopic examination was advisable to supplement the Roentgen-ray findings.

Bronchoscopy.—A large quantity of very foul pus was projected through the bronchoscope just as soon as it was inserted. After aspiration of the pus its source was found to be the left bronchus. Aspirating the pus as the tube advanced downward the suppurative focus was found to be in the left lower lobe. The bronchi of smaller size were found to be somewhat dilated; the spurs between branch bronchial orifices were found very much thickened; the mucosa was intensely inflammatory, in places the epithelium was eroded, and granulations were present in patches. Aspiration of the pus was continued until it failed to reappear on coughing. Separate specimens of pus were obtained from the upper and the extreme lower portions of the tracheo-bronchial tree; the specimen from the peripheral bronchi was obtained in a separate collector. Bacteriological examination of the pus obtained from the upper portions of the tracheo-bronchial tree revealed a great variety of micro-organisms including pyogenic and saprophytic organisms. The pus obtained from the peripheral bronchi in the small collector was found to be swarming with Vincent's organisms. Great improvement followed repeated aspirations, with local application of arsphenamin to the suppurative focus in combination with the intravenous administration of neo-arsphenamin. This patient is still under treatment and is still improving. We have had quite a number of cases of suppurative diseases of the lung due to Vincent's organisms [36]. This particular one is inserted here because it illustrates the way in which conflicting diagnoses may be cleared up by bronchoscope. (1) There was an old history of foreign body. (2) One roentgenologist had reported the presence of a shadow which he believed to be a pin; this was disputed by other roentgenologists. (3) The bronchoscopic findings showed clearly that the pus from the suppurative lesions right down in the suppurative focus was swarming with Vincent's organisms; whereas the pus aspirated from the trachea did not show the organisms, nor were they shown by any of the examinations of the sputum. This of course does not mean that they were not present in the sputum; it would be quite possible to overlook them in the large quantity of sputum that was produced. The technical difficulties in finding them in the sputum were very much greater than in the specimens of pus taken right from the focus where Vincent's organisms predominated. Be this as it may, the clinical fact is that the organisms were found in the specimen of pus that was taken bronchoscopically from the suppurative focus after all the flood of superjacent decomposed pus was removed. (4) The good effect from the use of arsphenamin in Vincent's infection of the bronchi is shown by this case, but at the time of reporting, the patient, though very much improved, is not yet cured. In other similar cases, however, satisfactory results have been obtained in almost all. Just how much of the effect is due to the local application of the arsphenamin and how much to the intravenous medication (from underneath, as one might say) it is impossible at present to determine. The solution for application to the bronchi was prepared by dissolving 0·1 grm. of arsphenamin in 5 c.c. of distilled water. This solution was applied by means of a dripping gauze sponge held in the bronchoscopic sponge-holder.

Case VII.—Infection by Vincent's organisms in an old epithelialized cavity in the lung.—A man, aged 31, came to us because of very profuse hæmorrhages from the lung, accompanied by foul expectoration. Ten years previously I had removed a piece of bone of nine years' sojourn from his lung by bronchoscopy. Following the removal he made a complete recovery, and was symptom-free for eight years. Then, following an influenzal infection, suppuration had gradually reappeared, and was accompanied by severe hæmorrhages. The patient was extremely anæmic, and preparations were made for transfusion. It was deemed best, however, to do a diagnostic bronchoscopy. A cicatricial stricture was found in the right lower lobe bronchus in the position from which the foreign body was removed ten years before. (Fbdy. 608.) A quantity of foul pus was coming up from below the stenosis. This was aspirated. So far as I could see through the stricture, the cavity was filled with granulation tissue, from which blood was oozing in quantities. Aspiration was continued until the blood withdrawn seemed to be entirely free from pus.

Bacteriological examination.—The last of the pus removed from the abscess cavity was

found to be swarming with spirochætes. Repeated examinations of the sputum failed to show these organisms.

Histologic examination.—A number of the fungations were removed from the interior of the abscess cavity, but none showed anything other than inflammatory and granulation tissue.

Progress.—After the first bronchoscopic aspiration the patient's condition began to improve. Repeated bronchoscopic aspirations were followed by continued improvement. A few additional hæmorrhages occurred, but at the end of three months of treatment the patient no longer brought up any sputum, had gained twenty-five pounds in weight, and seemed perfectly well. He has remained well during the two years that have intervened since.

Comments.—It seems probable that as a result of prolonged sojourn of the bone (nine years) the old abscess cavity that remained after removal of the bone was lined with epithelium that had no cilia; hence the defensive powers of the tissue in that region were very much diminished. When the patient was exposed to invasion by Vincent's organisms, secondary to the influenzal attack, possibly by secretions inspirated from the mouth during sleep, this weak point in the defence became the site of a spirochætal suppuration. Repeated bronchoscopic aspirations probably restored the defensive powers of the lung, and re-epithelialization of the entire cavity (as shown by subsequent bronchoscopic examinations) resulted. This is the only case that we have had in which the spirochætal invasion followed the cure of a suppuration due to a foreign body after the foreign body was removed; but in quite a number of cases in which a pulmonary abscess was cured by bronchoscopic aspirations a re-infection followed, and spirochætes were found. In some cases arsphenamin was used.

Case VIII.—Spirochætosis of the bronchi: recovery after bronchoscopic aspiration and arsphenamin locally and intravenously.—A native of Siam, aged 50 years, in the diplomatic service, had cough, foul expectoration, and occasional hæmoptysis. Bronchoscopy was requested by Dr. Joseph Bryan, of Washington. The patient had first noticed a cough about two years previously. After a time symptoms of pleurisy and pneumonia developed; the patient became ill and was confined to bed. The temperature was said to have been quite high at that time, but since, it has been only moderate; the exact amount of weight loss was undetermined. Professor McCrae reported as follows: "The patient is quite thin and has a frequent cough, but dyspnœa is not marked. Thoracic expansion is not particularly marked, but is distinctly less on the left side both anteriorly and posteriorly. Vocal fremitus over the lower left thorax seems rather diminished. There is dullness on percussion over the lower left thorax, but over the lower left interscapular region the note shows less dullness than below. On auscultation, the right side seems clear and the breath sounds are comparatively feeble on ordinary breathing. Over the upper part of the lower left lobe posteriorly, the breath sounds are almost amphoric with marked nasal quality to the voice sounds, rather suggestive of cavity in the locality. Below, the breath sounds are very distant, and a certain number of râles are heard, but they are not very numerous. The patient has brought up 180 c.c. of sputum. This is quite foul, blood-streaked and tends to separate in three layers."

Comments.—This case illustrates a frequently observed circumstance, namely, that spirochætes can be found in the secretions removed directly from the purulent focus in cases in which they cannot be found either in the sputum or in the flood of pus in the trachea and larger bronchi. In these cases there is stagnation of pus. The patient often brings up in the sputum pus that has been lying in the bronchi for weeks. It may be that during this period of stagnation the saprophytic changes cause a disappearance of the spirochætes, or it may be that the spirochætes are more difficult to find in a great quantity of pus diluted with saliva, and pus produced by suppuration in the mucosa or cavitary walls of regions possibly not affected by the spirochætal invasion. This case seems to corroborate the findings in other cases as to the efficiency of arsphenamin in the treatment of spirochætal infection of the bronchi even when the suppurative process has gone on so far as cavity formation.

Pulmonary mycoses.—The great usefulness of the bronchoscope in the diagnosis of these conditions is due to the fact that practically all fungi to be found in suppurative pulmonary foci are found also in the mouth. It is therefore difficult, if not impossible, to be certain that the organisms found in the sputum are really from the bronchi. Furthermore, there is no certainty on the negative side. It is exceedingly common at the bronchoscopic clinics to find organisms in the bronchoscopically removed secretions that have been repeatedly searched for in vain in the sputum. We are not at all sure as to the explanation of this; but it is a well-established clinical fact. It is true that even in the bronchi moulds may exist in great numbers as saprophytes or secondary invaders; but even so, they or their products probably are perpetuating factors. Fortunately the diagnosis by the bacteriological examination of secretions removed directly from the suppurative focus in the lung without contamination with the secretions of the mouth, is dependable negatively and positively. When the fungi are saprophytic, or secondary invaders, they disappear quickly after bronchoscopic aspirations have stopped stagnation. This clinical fact is well established by observation on a large number of patients under bronchoscopic treatment by many different assistants and pupils.

Actinomycosis.—Three cases of pulmonary actinomycosis have been observed at the bronchoscopic clinic. In two of these the organisms were first found in the secretions removed bronchoscopically. The following report is illustrative:—

Case IX.—Actinomycosis of the lung. Diagnosis made from bronchoscopically removed secretions.—A dealer in grain, aged 44, was referred with a tentative diagnosis of bronchiectasis. He had had slight nasal discharge and slightly productive cough as long as he could remember. Within a year there had been an increase of sputum and it became foul and occasionally blood-streaked. Sputum examinations were reported as "mixed infection, no tubercle bacilli or spirochætes seen." Bronchoscopic aspiration removed a great quantity of foul pus from the trachea. Both bronchi contained pus, but the greater quantity came from the right side. The bronchial mucosa on this side was intensely inflammatory and granular. Just below the middle-lobe orifice the lower-lobe bronchial stem seemed to be entirely occluded by a yellowish, granular mass of material. It seemed to be an intrusive cheesy gland, and on this supposition all loose material was entirely removed. When the removed material was examined it was found to contain many groups of the clubbed ray-fungi typical of actinomycosis. Nasal and general examination failed to reveal any other actinomycotic foci. The patient returned to the care of his family physician and died about a year later of pulmonary suppuration and intra-abdominal abscess. Consent of the patient to abdominal exploration and of the relatives for necropsy were both unobtainable.

Blastomycosis.—It seems probable that most of the patients with this disease die under a diagnosis of pulmonary tuberculosis. The exceptions are the cases in which a dermal lesion leads to the diagnosis. Mycelia are not usually present; the blastomyces are easily overlooked if the smears are stained. In one case at the Clinic the lesion was apparently primary in the larynx. The laryngeal lesion looked as though it might be luetic or malignant; it was too deeply and strongly red to be tuberculous. The serologic test was negative. A specimen removed from the larynx was found by Dr. B. C. Crowell to contain blastomyces. A tracheotomy had been done to prevent asphyxia before the patient came to the Clinic. Just before the patient came in a dermatitis had developed around the tracheal opening and it was found to be blastomycotic in character. Later a mycotic pulmonary suppuration developed, but this has not progressed; possibly because the patient has had continuous treatment with potassium iodide. This remedy seemed to cure the dermal, and to improve the laryngeal lesions.

Case X.—Blastomycosis of the lung; diagnosis made from bronchoscopically removed specimens.—A man, aged 36, a book-keeper, had been treated as tuberculous, but during two years no tubercle bacilli could be found in the sputum. Bronchoscopic examination

revealed a mass of granulation tissue occluding the right lower lobe bronchus. This tissue was removed with ball-forceps and was found to contain many blastomyces but no mycelia. Cultures from a piece of tissue required a month to show evidence of growth, but, finally, growths were typical of blastomycosis.

Case XI.—Blastomycosis of the lung associated with pulmonary tuberculosis and blastomycosis of the œsophagus.—A man, aged 34, developed difficulty in swallowing. Œsophagoscopic biopsy showed the stenotic lesion to be blastomycotic. Increasing cough with purulent blood-streaked expectoration of sputum negatively reported for tuberculosis and fungi, led to a request for a bronchoscopy. The last of the secretions removed from the left lower lobe contained numerous blastomyces. Subsequently pus bronchoscopically removed from the upper lobe bronchi was found to contain tubercle bacilli. The patient grew slowly worse; the tuberculosis and the blastomycosis both progressed, though the patient was living when last heard from.

Comment.—Mycotic organisms as secondary invaders are not uncommon in tuberculosis; but in this case the blastomycotic lesion of the lung seemed to precede the tuberculosis, and blastomycosis of the œsophagus apparently preceded both.

Case XII.—Blastomycosis of the lung.—A man, aged 40, a farmer by occupation, had been spitting up pus and losing weight for over a year. There were afternoon fever, malaise, clubbing of the fingers. He was suspected of having a pulmonary tuberculosis, but notwithstanding the fact that there was a considerable amount of foul purulent expectoration, tubercle bacilli could never be demonstrated. A bronchoscopy was requested in the hope of finding the bacilli in a specimen to be removed from the deeper portions of the lung, and especially from the left upper lobe bronchus, because the Roentgen-ray examination and the physical signs indicated that region as the one affected. At bronchoscopy a considerable amount of pus was found around the orifice of the left upper lobe bronchus, and a quantity of this pus was aspirated into the collector. No tubercle bacilli were discovered but great quantities of blastomyces were found. There were no mycelia present in the secretions removed; but after a long time a growth by culture was obtained and in this growth the mycelia were abundant. There were no cutaneous or laryngeal lesions found in this patient up to the time he disappeared from observation. Potassium iodide was advised but its use was probably neglected.

Pneumonia.—Bronchopneumonia is often relieved promptly at the Clinic by bronchoscopic aspiration, as shown by elsewhere reported cases. There is much evidence to show that the air-hunger in lobar pneumonia is due to obstruction of the bronchi by secretions. Coryllos and Birnbaum have shown that pneumonia is in many cases primarily an obstructive atelectasis relievable by bronchoscopic aspiration.

Adenopathy and Anthracosis.—Compression by glandular masses is often seen bronchoscopically. That the compressive mass is an adenopathy can be determined positively with the bronchoscope after intrusion of a suppurative gland into the bronchus. Prior to that time the character of the mass will be based on inference from the general medical examination, the Roentgen-ray examination and the laboratory findings. As noted in a recent communication [37] this compressive stage may show obstructive emphysema or obstructive atelectasis, in the beginning; but later suppuration in the tributary lung-area follows from annihilation of the defensive power of the lung. When the compressive stage is succeeded by the intrusion of the glandular suppuration through the wall, bronchoscopic clearance of the obstruction is usually indicated, and in benign conditions it is not rarely followed by restoration of health. Moreover, examination of the removed material will clarify the diagnosis, as in the following case.

Case XIII.—Pulmonary suppuration secondary to bronchial obstruction by the intrusion of an anthracotic gland.—A man, aged 65, a coal-miner by occupation, was referred for determination of the source of pulmonary hæmorrhages. There was a history of a productive cough intermittently since whooping-cough in early childhood. Recently there had been

spitting of blood, dyspnœa, and wheezing. Roentgen-ray examination by Dr. Willis F. Manges: "There is ragged, irregular density in the right root area. Comparison with earlier films would make one feel more in favour of infection than malignancy." Bronchoscopy revealed obstruction in a branch of the right lower lobe bronchus from which blood was oozing. A fistula led into a small cavity containing black material; a very foul odour came from the bronchoscope as this pocket was being examined. Black material was removed with ball forceps. The report of Dr. Crawford on the histology of the material: "Examination of sections from the small pieces of tissue reveals that they are composed of very dense fibrous tissue in which there is a large amount of black, closely packed pigment. One of the pieces of tissue is partially covered by a thin, stratified, squamous epithelial membrane. In one small area there is a slight thickening and hyperplasia of the surface epithelium and there is what seems to be epithelium from the remains of the mucous glands in one area of the tissue. This epithelium is slightly irregular and hyperplastic, but no evidence of malignancy is observed. Diagnosis: fibroid and anthracotic tissue."

Six months have elapsed and there has been no hæmorrhage since the clearing out of the anthracotic material from the cavity communicating with the right bronchus.

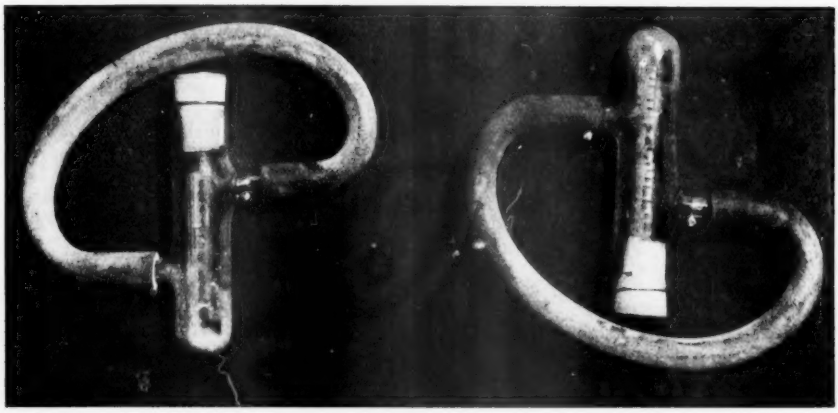

FIG. 3.—Typical secretion bronchoscopically aspirated from a patient with asthma. The viscosity is so great that air hunger is extreme. Small masses of it often act as check-valves resulting in a pumping of air out of the lung. Great relief follows bronchoscopic aspiration. Later in the progress of the disease, if not treated by bronchoscopic aspiration, the secretion becomes more and more purulent. At the right the collecting tube is shown inverted; the secretion is so viscid it will not run down.

Asthma.—Time and space forbid consideration of this enormous subject. Only a few of our bronchoscopic observations need be mentioned here. (1) In asthma, as the internist understands the term, the patient usually has a very thick tenacious mucoid secretion that, when aspirated into a collector, will not run down the smooth glass surface when the collector is inverted (fig. 3). (2) Bronchoscopic aspiration of this secretion gives the patient complete subjective relief for a longer or shorter time. (3) Vaccines prepared from the material bronchoscopically removed are often of greater benefit than those prepared from sputum. (4) Over 90% of the patients sent in with a diagnosis of asthma have organic disease. (5) More than half of them do not have asthma, but wheeze from obstruction of the trachea or larger bronchi. (6) The obstruction may be due to foreign body, tissue or secretions; the largest group is foreign body, the next largest malignant disease. (7) Every medical student should be strongly impressed with the aphorism: "All is not asthma that wheezes."

Bronchiectasis.—The experience at the bronchoscopic clinics of Philadelphia and Pittsburg corroborates that of bronchoscopists everywhere in regard to the

usefulness of bronchoscopy in bronchiectasis. Excellent reviews of this subject have been published by Ewart Martin, Soulas [30], Orton, Raffo [39], Kernan, Yankauer, Myerson, Imperatori and others. As McCrae [35] has said: "Bronchoscopy is of value, used early; but *early* must be stressed. This means early diagnosis, which is very rarely made. We may be able to prevent advanced bronchiectasis by early recognition and prompt bronchoscopic treatment."

In advanced cases the patient can be made more comfortable by bronchoscopic aspiration, which will stop prolonged stagnation and thus control the odour that renders him ever conscious of the annoyance he causes everyone near him.

Accessory nasal sinuses and bronchiectasis.—Statistics and observations at the Philadelphia and Pittsburg clinics fully corroborate the experience of clinicians everywhere as to the association of bronchiectasis and disease of the nasal accessory sinuses. We have also come to base our prognosis to some extent on the curability of the sinus disease. If a patient has an incurable focus in the sinuses it is useless to expect more than palliation of the secondary suppuration in the bronchi. This palliation may be worth while to the patient, especially as bronchoscopic aspiration lessens the odour or causes it to disappear.

Pulmonary Abscess.

Acute pulmonary abscess.—The acute cases in which bronchoscopy was considered advisable were ætiologically attributable to the usual factors, influenza, pneumonia, operations, parturition, acute infections, and so on. A large majority, however, followed the tonsil operation, and it is in this group that the best results have been obtained from bronchoscopic aspiration, probably because early opportunity for treatment was most often afforded. It is of this group that we have the largest statistics.

Post-tonsillectomy pulmonary suppuration.—Statistics as to pulmonary abscess complicating operations on the tonsils, incomplete as they are, show curious national differences. In some countries, the operators upon tonsils have not seen a single case, whereas in the United States there have been a great many cases. By this I do not mean that the complication is a very common one; indeed, considering the enormous number of tonsillectomies that are done, it must be considered relatively a rare complication. I have not done a tonsillectomy for over twenty years. If anyone prior to that time had asked me if I had ever had a patient who developed suppurative disease of the lung following a tonsillectomy I should have replied in the negative, and it is possible that I might have given inferential reasons for my freedom from such a complication; yet in retrospect there are quite a number of cases in which I now feel suppurative disease of the lung resulted from my tonsil operation. Therefore I cannot say that I did not see such complications, but rather that I did not recognize the connection between the suppurative disease of the lung and my operation which preceded it. Pulmonary abscess is, regardless of its cause, such a serious disease that every effort should be made to determine every factor in the ætiology. If any of these factors concern the technique, the instruments, the methods of operation or after-care it is necessary that proper steps be taken to eliminate such causative factors. Considering the frequency with which the tonsil is probably the primary infective focus in cases of pulmonary suppuration in patients who have not had a tonsillectomy it is possible that some of the post-tonsillectomy patients would have had pulmonary suppuration sooner or later even if no operation had been done. However, as Dan McKenzie has so well expressed it, "These accidents are disconcerting because the post-operative illness is out of all proportion to the pre-operative conditions."

The following fragmentary notes will afford some idea of the clinical features of this type of pulmonary abscess, and its response to bronchoscopic treatment. Though not all of the cases may be considered acute, they are grouped together because they all occurred as a complication of tonsillectomy.

Case XIV.—Man, aged 40. Post-tonsillectomy abscess of the left upper lobe. Duration of suppurative symptoms eight months. After eight bronchoscopic aspirations the abscess had completely disappeared. (Dr. Aucoin.)

Case XV.—Man, aged 30. Post-tonsillectomy abscess. Patient came for treatment seven months after the onset of a suppurative lesion of the lung. During fourteen months seventy-eight bronchoscopic aspirations were done by different members of the staff. Though the patient had many hæmorrhages, and was several times in a very serious condition, a perfect cure resulted. We had despaired and had tried to send the patient back to the internist who referred him to us. The patient desired, however, and the internist advised, that the bronchoscopic aspirations should be continued. The patient insisted that he felt better when aspirated twice a week. The outcome justified the opinion of the patient and the internist. (All Members of Bronchoscopic Staff.)

Case XVI.—Post-tonsillectomy abscess. Man, aged 22. Symptoms came on three days after tonsillectomy. Patient admitted on sixth day. Bronchoscopy showed pus coming from posterior division of left lower lobe bronchus. There was an inflammatory process of moderate degree in the bronchus, indicating the probability of an inspirated infection. Gained 25 lb. and was symptomatically well. Seven bronchoscopies. (Dr. Tucker.)

Case XVII.—Post-tonsillectomy abscess showing fluid level in the roentgenogram taken on admission. Complete disappearance of the pathological shadows followed five bronchoscopic aspirations. (Dr. Clerf.)

Case XVIII.—Post-tonsillectomy abscess of the left upper lobe. Cure after four bronchoscopies. (Dr. Lukens.)

Case XIX.—Man, aged 27. Post-tonsillectomy pulmonary abscess, left upper lobe. Admitted three weeks after the tonsillectomy. The symptoms and the pathologic shadows shown in the roentgenogram disappeared after eleven bronchoscopic treatments. (Dr. C. L. Jackson.)

Case XX.—Boy, aged 13. Post-tonsillectomy pulmonary abscess, left upper lobe. Bronchoscopic aspiration begun one month after onset of symptoms. Recovery after three bronchoscopic treatments. (Dr. C. L. Jackson.)

Case XXI.—Post-tonsillectomy abscess of the middle lobe. First bronchoscopy was done within thirteen days after onset of symptoms, which appeared five days after operation. A roentgenogram showed almost complete disappearance of the pathological shadows two weeks after the second bronchoscopic aspiration. A roentgenogram two months later showed the lung practically normal. There was no recurrence of the symptoms. (C. J. and Staff.)

Case XXII.—Post-tonsillectomy abscess of the right lower lobe. Pulmonary symptoms began in the first week following tonsillectomy. The patient was referred to the clinic one month later. Recovery after seven bronchoscopic treatments at weekly intervals. The patient gained 15 lb. in weight and was symptomatically well. (C. J. and Staff.)

Case XXIII.—Post-tonsillectomy pulmonary abscess in a man, aged 37. Patient was coughing up large quantities of pus. After the first bronchoscopy the quantity of pus increased slightly and then began to diminish. After a series of bronchoscopic treatments the symptoms entirely disappeared. The slight increase in quantity of sputum has often been noted; we regard it as indicative of improvement in spontaneous drainage, the first stage in the restoration of the defensive powers of the lung. (C. J. and Staff.)

Case XXIV.—Man, aged 50. Post-tonsillectomy abscess of the middle lobe, cured after five bronchoscopic aspirations. First treatment was six weeks after onset (Dr. Moore).

Case XXV.—A woman, aged 30. Post-tonsillectomy pulmonary abscess. After a series of bronchoscopic aspirations during a period of three months, the patient had gained 30 lb. in weight and was symptomatically well. The Roentgen-ray examination demonstrated a total disappearance of the pathologic shadows. (C. J. and Staff.)

The following case may be regarded as typical of the results of very early bronchoscopic aspiration. It occurred in a hospital where we have a well-equipped and organized bronchoscopic clinic. The laryngologist who did the tonsillectomy had seen so much of our work that he called upon me promptly for bronchoscopic aspiration the first day the child spat up foul pus and blood.

Case XXVI.—Post-tonsillectomy pulmonary abscess promptly arrested after bronchoscopic aspiration.—A boy, aged 4, was seized, four days after tonsillectomy, with great prostration, cough, foul and slightly bloody expectoration, and fever. Roentgen-ray examination showed

an abscess in the right lung. Three days later the abscess had increased in size, as shown in the middle illustration. Bronchoscopy was done; following it a third Roentgen-ray examination showed a diminution in the size of the shadow of the abscess. After two more bronchoscopic aspirations all the symptoms disappeared, and the child recovered perfect health. (C. J.)

Comment.—The prompt arrest of the rapidly progressing process was shown in the roentgenogram. In this, as in many similar cases, the question came up as to whether or not it was advisable to do a bronchoscopy with the tonsillar fossæ as yet unhealed. We have never found any retardation of healing processes as the result of a bronchoscopy done even within three days of the tonsil operation. Of course the fauces are still tender, which causes the patient more distress at bronchoscopy. But after a full week's interval usually the children do not mind any remaining tenderness. A result such as that in this case is not always obtainable. Occasionally a case is encountered in which everything seems powerless to restore the defensive powers of the lung, and the disease passes on into the chronic form, requiring many treatments to effect cure. These cases are relatively rare. Still more rare is the case of the fulminating type with a very extensive breaking down of pulmonary tissue that is rapidly fatal. In one such case, on the third day after tonsillectomy, there was a chill, followed by vomiting, profuse hæmorrhage and expectoration of foul pus containing fragments of necrotic tissue. The patient was moribund on admission, therefore no bronchoscopy was done. Autopsy revealed a septic infarct of a large vessel, with gangrene of the whole left upper lobe. Our statistics show that favourable results are obtained in nearly 80% of the cases of acute pulmonary abscess seen within less than four weeks of the onset. In such cases an opportunity for bronchoscopic drainage was given very early in the disease, when quick restoration of the defensive powers of the lung could be obtained before destruction of the cilia and very extensive tissue loss had taken place, and the invading bacteria had become entrenched behind a barrier where they were free to attack relatively defenceless outlying undrained tissue. The reason why so many of these acute cases were encountered is that they occurred in the practice of the laryngologists, who have seen enough of the results of bronchoscopic drainage to realize the advantages of prompt recourse to it as soon as the diagnosis is made. In the cases of acute pulmonary abscess occurring in general practice, recourse to bronchoscopy is often delayed until the condition has become chronic. At first I was inclined to think that the better results were obtained because of inspiratory origin in the post-tonsillectomy cases; but since the investigations of Fetterolf and Fox [32] I am not certain that all of the post-tonsillectomy abscesses are inspiratory infections.

Of 224 patients with pulmonary abscess following operations on the tonsil and upper air passages treated by bronchoscopic aspiration 136 (61 per cent.) were apparently well and symptom-free when last seen; 32 (13 per cent.) were unquestionably improved; 24 (11 per cent.) were worse or unimproved; 24 (11 per cent.) were referred to the surgeon. There were 8 deaths (4 per cent.) while the patients were under bronchoscopic treatment though none could be attributed to bronchoscopic treatment. The terminal phases were cerebral complications in 2, cardiac complications in 1, extension of the suppurative process in 3. One of the latter was of the fulminating type with rapidly extending pneumonitis and so-called gangrene of the lung. In such cases neither bronchoscopy nor, probably, anything else, offers any hope; therefore bronchoscopy was ill-advised.

The route of infection is as yet an unsettled question. Does the infection travel by the airway, the blood channels, the lymph channels, or by each in respective cases or by two or all combined? Fetterolf and Fox have shown how directly the blood channels lead from the tonsil to the lung; that lymph channels may carry infection either from the tonsillar fossæ or the endo-bronchial mucosa cannot be disproven; that the airway is a direct channel is obvious, but we have also the positive evidence

afforded by foreign body cases. We have bronchoscopically removed from the bronchi: part of a mouth gag, two nasal rasps, part of a tonsil forceps, a tonsil snare wire, a tonsil swab, a tonsil tampon and part of a tonsil knife [38]. In none of these cases did pulmonary abscess follow, but elsewhere discussed factors enter into consideration here. For practical work in clinical cases it is wise to use every possible means to prevent inspiratory infection. The best means of doing this is to aspirate blood and secretions after operation, through the laryngoscope, and if necessary through the bronchoscope.

Post-operative pulmonary abscess.—The following report is illustrative of the results of bronchoscopic treatment of pulmonary abscess following an abdominal operation.

Case XXVII.—Pulmonary abscess following cholecystectomy.—A man, aged 35. Following cholecystectomy, pulmonary symptoms suddenly developed, with expectoration of large quantities of foul pus. The patient was admitted to the bronchoscopic clinic two months after onset of symptoms. After four bronchoscopic treatments the patient was entirely free from symptoms and seemed completely restored to health. One point of great interest in connection with this case is that pulmonary abscess following abdominal operation has been usually regarded as embolic in origin. Probably this is the truth. It is therefore very interesting to know that bronchoscopic aspiration is quite as efficient a curative measure in pulmonary abscess of embolic origin as it is in the cases arising from inspiratory infection. It is therefore logical to conclude that bronchoscopic aspiration has taken the load off the cilia and has restored the defensive powers of the lung which were overwhelmed by the infective process.

Drowned lung.—It is of importance, at least it has seemed so to me for many years past, to make a distinction between a condition of drowned lung, on the one hand, in which the natural passages with intact walls are full of pus, and an abscess properly so-called, in which the walls have given away. If the bronchial obstruction to drainage can be removed bronchoscopically during the stage of drowned lung, recovery from benign conditions is prompt. If there is delay until the bronchial walls give way, recovery is slower and cicatrization is necessary for healing.

Pulmonary abscess, chronic.—The chief cause of chronic pulmonary abscess, it seems to me, lies in permitting the acute process to run on into chronicity. Early bronchoscopic aspiration should prevent this in many of the cases. The chronic abscess is curable by bronchoscopic aspiration, but a much greater number of treatments are required before the defensive powers of the lung are restored. When this stage of restoration is reached, the patient may go on to cure without further bronchoscopic aspirations. In all of these cases the patient should have general medical care and management, especially rest in bed outdoors, to build up a reserve. Vaccines prepared from material removed from the abscess are helpful. Focal infections in the nasal accessory sinuses, teeth, tonsils, or elsewhere should, of course, receive proper attention.

Post-pneumonic pulmonary abscess.—Many patients have been referred to the bronchoscopic clinic with the diagnosis of "post-pneumonic pulmonary abscess"; and in our records the cases are so classified because it has been impossible to determine in just how many of the cases the primary condition was a true lobar pneumonia. The following is an example.

Case XXVIII.—Man, aged 34. Pneumonia eight months before admission. Abscess right lower lobe. First bronchoscopy four months after onset of suppuration. Recovery after seventeen bronchoscopic aspirations. (Dr. Clerf.)

Diagnosis.

Bronchoscopy is indicated whenever the diagnostic question calls for specular examination of the lungs. In principle the bronchoscope bears the same relation to intrathoracic disease that the vaginal speculum does to pelvic disease. The

technique of its use requires special training; but once the technique is acquired, the procedure is such that no practitioner need hesitate to avail himself of the diagnostic information that only the bronchoscope can give.

Bronchoscopy supplementary to Roentgen-ray diagnosis.—As elsewhere mentioned, bronchoscopy is not a substitute for any other method of examination; it is simply an addition thereto. In no case would we think of doing a bronchoscopy until after a complete Roentgen-ray study, except, of course, in urgent cases; and quite often the bronchoscopy has merely confirmed the Roentgen-ray diagnosis. There have been other cases, however, in which Roentgen-ray diagnostic findings have not been conclusive without the supplementary information that could be afforded only by the bronchoscope. In still other cases the Roentgen-ray findings have been entirely negative; the proportion of this kind of case has been growing less and less each year, owing to the continued improvement in roentgenological technique and interpretation.

In most cases of bronchial obstruction the fact that there is obstruction can be demonstrated by Roentgen-ray examination; but the character of the obstruction is often not determinable by X-ray examination alone. This is a common occurrence at all the bronchoscopic clinics; a few examples of such cases are given in the accompanying reports.

In another class of case the Roentgen-ray has shown a shadow of what has been interpreted as an inflammatory process; but the cavity being filled with pus, there was no fluid level by which to demonstrate an abscess; in such cases bronchoscopic aspiration, by emptying the abscess, has shown the presence of a cavity and re-accumulation has produced a fluid level demonstrable by the shadows in a roentgenogram. The secondary suppurative processes at times have masked the shadows that would otherwise have been recognized as typical of malignant disease. Here again the endo-bronchial examination has supplemented the Roentgen-ray findings by local inspection and, usually, biopsy. Benign growths cause obstruction to the bronchi. When the growth was primarily endo-bronchial the Roentgen-ray examination has shown signs of bronchial obstruction of some one of the three types elsewhere herein mentioned. But the character of the obstruction has been determined in its early stage only by the bronchoscope, and it is the bronchoscope that has been the means of efficient treatment. None of the foregoing is in any way a depreciation of the diagnostic value of Roentgen-ray diagnosis. The kind of cases referred to simply show that justice to the patient requires that no diagnostic means be neglected; even when all are used, we often wish for additional information.

Pneumonography.—The first pneumonogram was made bronchoscopically with bismuth subcarbonate, and occasionally the bronchoscopic insufflation of this substance is the most useful method of obtaining a pneumonogram. Lipiodol is now more frequently used at the bronchoscopic clinic. It is by no means always necessary to use the bronchoscope for this purpose. In certain cases, however, the bronchoscope presents advantages. Secretions may prevent lipiodol from finding its way into the bronchi. It is very easy to remove obstructing secretions bronchoscopically from either bronchi or fistulæ leading to abscess cavities, and then to inject the lipiodol or insufflate the bismuth. Great precision of introduction into the desired region is rendered possible by the bronchoscopic method.

Prognosis.

Bronchoscopy has revolutionized the prognosis of suppuration due to foreign body. In the pre-bronchoscopic days the mortality was about 75%. Under modern bronchoscopic methods the mortality is probably not more than 2% or 3%.

The prognosis of suppurative disease of the lungs and bronchi of other than foreign body origin has been greatly improved by the addition of peroral bronchoscopic drainage to medical care and management. In suppuration due to foreign

body, recovery may be expected in over 95% per cent. of the cases. In some suppurative conditions, such as those due to benign growths and all bronchoscopically remediable forms of bronchial obstruction, the bronchoscope has been a life-saving measure that has reversed the unfavourable prognosis. This includes the majority of non-tuberculous and non-malignant diseases of the bronchi and lungs. In some cases of tuberculosis the prognosis has been improved also. Even in malignant disease some improvement in prognosis has followed bronchoscopic aid in diagnosis and treatment. A very great improvement in the general prognosis of pulmonary malignant growths would follow early and positive diagnosis; the only way to obtain this is by early bronchoscopy in all cases in which malignant disease is one of the diagnostic possibilities.

Treatment.

Summarizing the matter of bronchoscopic treatment of pulmonary disease, it may be said that it has a large field of usefulness. It is to be considered only as an aid to the physician and surgeon. In no case should other means be neglected. It often happens that medical care and management are sufficient to prevent the disease getting worse, but the patient does not improve. In many such cases the addition of bronchoscopic drainage will turn the tide. The local bronchoscopic treatment of infective suppurative diseases of the lungs consists largely in peroral drainage and in thus restoring the defensive powers of the lung; but in addition, direct local applications of arsphenamin are efficient in spirochætal and Vincent's infections. At our clinics local medication has been used in addition to bronchoscopic aspiration in cases of suppuration due to mixed pyogenic infections; just how much it has contributed to the cure of the bronchial suppuration in these cases has not been determined. The harmlessness of the various medicaments has, however, been abundantly demonstrated.

Bronchoscopic aspiration, if used promptly, is successful in the restoration of function in cases of post-operative atelectasis. In these cases the obstruction causing the collapse is in the form of secretions. The bronchoscopic aspiration of these secretions results in very prompt re-expansion of the lung. In a certain proportion, probably one-half of the cases, the thick secretions re-accumulate, and re-aspiration is required. A very good illustration of the efficiency of this form of treatment is afforded by the following case.

Case XXIX.—Post-operative atelectasis.—A boy, aged 8, was hospitalized for the treatment of a cicatricial stricture of the œsophagus due to the swallowing of lye. Œsophagoscopic treatment had resulted in the complete cure of the stricture. The abdominal surgeon was called upon to close the gastrostomic fistula, which a prolonged test had proved unnecessary because of the restoration of the patency of the œsophagus. Seventy-two hours after operation for plastic closure the child became seriously ill, with elevation of temperature and very rapid pulse. Physical signs and Roentgen-ray examination showed that the left lung was completely collapsed. Bronchoscopy revealed the left main bronchus filled with thick tenacious secretions. Bronchoscopic aspiration of this secretion resulted in the breath sounds reappearing all over the previously collapsed lung within a few minutes; and after one hour the percussion-note began to improve. The immediate betterment in the general condition of the child was remarkable. The colour, temperature, pulse and respiration soon became normal. A slight reappearance of the symptoms required a repetition of the bronchoscopic aspiration, but progressive improvement followed, and recovery was uneventful.

The cure of suppurative diseases of the lung by the bronchoscopic removal of endo-bronchial benign growths is, next to the removal of foreign bodies, one of the most brilliant achievements of bronchoscopy. There have been 187 cases of endobronchial removal of inflammatory and benign growths in the bronchoscopic clinics

of Philadelphia and Pittsburg. In nearly all these cases the suppurative process was arrested.

Vaccines.—Many of the failures to obtain satisfactory results from vaccine therapy are due to the use of vaccines prepared from secondary invaders. Our results have been incomparably better since we have rejected all the pus from the trachea and the bronchi above the focus. The focal pus is separately aspirated for bacteriological study and the preparation of vaccines, because it usually contains the most important organisms.

Postulates.

The following notes are offered, not as conclusions, but as postulates for discussion :—

(1) Bronchoscopic aspiration may seem new, but in principle it is really very old. Prehistoric man probably opened such superficial abscesses as he could reach with a flint. Certainly, Hippocrates advised drainage of pus in accessible locations. The only new thing about bronchoscopic aspiration is the discovery of the fact that pus in the lung can by this means be drained through the mouth without danger and without general anæsthesia.

(2) The disappearance of the odour, as well as the saprophytic organisms, from the pus, and the improvement in the local and general conditions of the patient after a series of bronchoscopic aspirations, supports the view that the saprophytes or their products are important perpetuating factors in chronic suppurative disease of the bronchi and lungs.

(3) Bronchoscopic aspiration is indicated for treatment : (*a*) to prevent stagnation ; (*b*) to restore the defensive powers of the lung, especially the ciliary action ; and (*c*) to remove obstruction if present. It is also indicated for prophylaxis, to prevent acute suppurative processes from becoming chronic.

(4) Greatly increased efficiency in vaccino-therapy can be obtained by the use of vaccines prepared from residual pus obtained directly from the suppurative focus in the lung after the superjacent stagnant pus has been aspirated off. Such specimens are of course uncontaminated by secretions from the mouth.

(5) The bronchoscopist is a specialist; his work is subsidiary to that of the practitioner, internist or pædiatrician, whose broad viewpoint is needed in every case of pulmonary disease, whether it be generally classed as medical or surgical.

(6) In a serious morbid complex such as is so often presented by a patient with symptoms of suppurative disease of the lung, the close co-operation of the internist, the surgeon, the roentgenologist, the pathologist, the rhino-laryngologist, and the bronchoscopist will accrue to the best interests of the particular patient and to the advancement of medical science.

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Section of Neurology.

President—Mr. LESLIE PATON, F.R.C.S.

[*October* 9, 1930.]

PRESIDENT'S ADDRESS.

Classification of the Optic Atrophies.

By LESLIE PATON, F.R.C.S.

FOR my address to-night I have thought it may be of interest to pass in review a general subject like optic atrophy which, perforce, has come much under my observation during the years I have worked at Queen Square. I propose to deal, mainly, with the classification of optic atrophies, and, incidentally, with one or two rarer or less known causes of optic atrophy. Naturally, most of what I have to say is of a most elementary nature, but it is sometimes wise to go back to elements.

Optic atrophy is essentially a degeneration of the nerve fibres, with consequent loss of function. Clinically it shows itself in an increasing pallor of the optic disc, but the pallor and general appearance of the disc may show considerable variations according to the nature of the optic atrophy, and the loss of function may also manifest itself in a variety of ways. There may be marked deterioration of visual acuity with good peripheral fields, or the reverse condition—quite good central acuity with marked peripheral contraction of the fields. The colour fields may be affected to a much greater extent than the white fields. The restriction of the fields may be general or segmental, or in the nature of a ring scotoma, or a central scotoma, or paracentral scotomata. The power of dark and light adaptation may be diminished or slowed down. There may be alteration in the reflex pupil reactions. In ordinary clinical work the variations of the visual fields are the most important from the diagnostic standpoint and help most in determining the cause of the atrophy.

There may be great variations in the colour of the disc within physiological limits. The disc of the old is usually paler than the disc of the child, the disc of the myope paler than the disc of the hypermetrope. In some anæmias the disc may be very pale without any optic atrophy and, further, a pathologically pale disc may exist without any discoverable loss of function. I have seen a case in which there had been patches of disseminated sclerosis in both nerves. After recovery there was full $\frac{6}{5}$ vision, no evidence of field affection, either peripherally or centrally, but the discs were paper-white in colour.

Furthermore, there may be great variations in the extent to which the vessels are affected in different types of atrophy. When it is consequent on retinal degenerations the diminution in the calibre of the arteries is a very characteristic feature, and in the final stages, they become reduced to mere threads. In tabes, on the other hand, the calibre of the vessels is often, seemingly, normal, when the nerve-head shows an advanced condition of atrophy and when the visual functions are markedly diminished.

In dealing with a very complicated series of cases some method of classification is essential. The attempt, however, to attain too great simplicity can only produce

results which are misleading and harmful to the progress of knowledge. A true classification can only be made when the essential nature of all the subjects to be classified is thoroughly known and their inter-relationships understood. A perfect system should be completely inclusive and completely exclusive. It should include all the cases in one or other of its subdivisions and each case should be included in one subdivision and excluded from all the others. This second requirement can never be completely satisfied. Even one of the most satisfactory classifications, that of the elements on an atomic basis, has been found in modern times to fail to satisfy it. Yet we must constantly strive to indicate the relations of one form to another as closely as possible by our system of classification. We must constantly, like the professor in Heine's sarcastic sketch, be shuffling our labels from one plot to another as we become more intimate with the intrinsic nature of each case. Unfortunately, the boundaries of our plots are only vague and ill-defined and we must be content with a pragmatic scheme. The question then arises as to which characters are best suited to give a scheme which will be sufficiently inclusive of all the cases of which the nature is known, and sufficiently exclusive to allow us to differentiate between them. But before we proceed to construct our system I wish to get rid of our present system. Nothing can be more misleading than the use of the terms " primary " and " secondary " as they are commonly applied to cases of optic atrophy. If we must use the terms at all, we must try to use them with a proper understanding of their connotation. What is a primary atrophy? Surely, if terms have any meaning at all, it must be that form of atrophy of the optic nerve in which the toxin or trauma directly acts on the nerve fibre and kills it. A secondary atrophy will be, then, that form in which the death of the nerve fibre is the consequence of inflammation or degeneration of other structures on which the nerve is dependent, or which, from their anatomical relationships to the nerve, can produce injury to its fibres. But these are not the meanings given to the term in our textbooks. There, a primary atrophy is defined as one in which the optic disc shows no evidence of any antecedent papillitis or œdema. But why should we differentiate between the atrophy produced by an optic neuritis affecting that small portion of the nerve included in the disc and immediately behind the disc and a similar neuritis affecting the nerve behind the entry of the central vessels? True primary atrophies are probably limited in number. The great bulk of cases included in this class results from inflammations and degenerations and growths affecting structures on which the nerves depend.

A secondary or consecutive atrophy is said to be one in which the optic disc shows evidence of an antecedent œdema or papillitis. But I am sure any of you who have been in a position to watch either a papillœdema or a papillitis from beginning to end must have seen cases where, after the subsidence, no trace of the preceding œdema has been left, or where the disc exactly resembles the disc of a so-called primary atrophy, with clear edges, undisturbed retinal pigment and lamina cribrosa showing in the physiological pit. Furthermore, what are we to say of these cases where a papillœdema has occurred, but has not been the cause of the optic atrophy? Sometimes, as may happen in pituitary or suprapituitary tumours, a papillœdema may occur in a case in which a pressure atrophy is already present, or, again, it may happen that the papillœdema is present first but the atrophy results from pressure on the intracranial portion of the nerve.

I do not wish to leave you in any doubt on the subject of my opinion on these two terms. I wish to see them abolished entirely from the textbooks. I think they are worse than valueless. They are misleading. They are like that blessed word " Mesopotamia "—comforting only to the ignorant. The only meaning they can have is an error. Many years ago, Dr. Hughlings Jackson told me that it took twenty-five years to get a fresh idea into an English textbook and fifty years to get an error out of it. Twenty-five years are passing and I believe we may soon hope

to see the term "optic neuritis" used in its proper connotation, but I fear it will be many years yet before the use of these terms "primary" and "secondary" is abandoned.

We can now proceed to examine briefly the basis on which a more satisfactory classification may be founded.

The optic nerve is a tract belonging to the central nervous system and it suffers the same pathological changes as other white tracts do, only modified in particular ways by the peculiarities of its anatomical relationships. Atrophic changes in it may result from inflammations which may be acute or chronic, from degenerations which may be the result of mechanical injury, pressure or traction, or they may be the result of interference with the blood supply, or of the action of toxic agents. The optic nerve may take part in systemic degenerations affecting other portions of the white matter of the central nervous system where the cause remains unknown. The lesion, in some cases, may directly affect the nerve fibres. In other cases, the meninges and interstitial tissue may first suffer and the degeneration of the nerve fibres may be consequent on that, or the degeneration of the nerve fibres may follow on degeneration of the ganglion cells from which they arise.

The activities of these various causes are modified by the different anatomical relationships of the nerve in different parts of its course. Some of them may act on the nerve fibres in general, and are not locally restricted. A patch of disseminated sclerosis may affect any portion of the nerve where there is a myelin sheath, and if it affects the anterior portion of the nerve it may produce an œdema of the papilla, so that we may find any part of the nerve affected from the papilla to the chiasma. Certain toxins seem to affect the nerve diffusely; probably the aryl-arsenates do so. The site of action of other toxins such as tobacco and carbon bisulphide has not definitely been determined, and, unfortunately, there remain a proportion of cases of atrophy of unknown origin. So our first basis of classification will be into: (1) Atrophies of localized origin. (2) Atrophies of diffuse or indeterminate origin. (3) Atrophies of unknown origin.

As, however, by far the largest number of cases belong to the first class, it is mainly with the subdivisions of this class that we have to deal.

As I have said, the optic nerve is not a peripheral nerve but a portion of the central nervous system, a tract of white matter anatomically, embryologically and physiologically comparable to any of the other columns of white matter in the central nervous system, subject to the same diseases and responding to these diseases by the same type of reaction. The main bulk of cells from which its fibres arise lie in the retina, so that the main bulk of its fibres are ascending fibres, but not all. There also exist descending fibres whose ganglion cells lie in the higher centres and whose function may possibly be concerned in dark adaptation. Furthermore, not all the ascending fibres have the same destination. Some are visual fibres whose primary relay station is in the external geniculate ganglion. Others are light fibres, with a primary relay station in the anterior corpus quadrigeminum. These three types of fibres seem to have different sensibilities to the action of different toxins and suffer at unequal rates.

Now this nerve may be affected at any part of its course from its origin in the retina to its end in the chiasma, where it ceases to be called a nerve and is called by its proper name—a tract.

We can most conveniently subdivide the nerve into three portions: (1) The retinal. (2) The papillary. (3) The retrobulbar.

This last portion may be further subdivided into: (*a*) Orbital. (*b*) Foraminal. (*c*) Intracranial.

The primary lesion, then, may affect the nerve in any of these different portions.

We have, then, three main classes of optic atrophy of localized origin: (1) Retinal. (2) Papillary. (3) Retrobulbar. And the third class has three subdivisions: (*a*) Intra-orbital. (*b*) Foraminal. (*c*) Intracranial.

In each of these main divisions, atrophy may be the after-effect of inflammations, acute or chronic, or of degenerations. These degenerations may be locally produced—for example, by pressures, or tractions—or they may be systemic degenerations of unknown origin, or consequent on vascular insufficiency. The inflammations can further be subdivided into parenchymatous and interstitial forms.

The clinical appearances of a typical case of each kind present certain distinguishing features, though I have already hinted that too much reliance must not be placed on these points.

Group 1.—Atrophies consequent on Retinal Degenerations.

These can give rise to little doubt, as there is present the obvious ophthalmoscopic picture of the primary retinal lesion. The disc usually presents a clear outline and a waxy surface, as if it had been filled in with beeswax, but the most important feature is the extreme diminution of the calibre of the vessels.

In this group are found the primary atrophies of the retina—retinitis pigmentosa, amaurotic family idiocy, cerebromacular degeneration—and the numerous forms of secondary retinal atrophy consequent on retinal and choroido-retinal inflammations and vascular degenerations which may affect either the peripheral or the central portions of the retina, or both simultaneously. The essential cause of the atrophy of the nerve in this group is the degeneration of the ganglion cell from which the nerve fibre originates. This may follow on a neuro-retinitis, or a choroido-retinitis, or it may be a systemic degeneration, as in the case of the various forms of cerebromacular degeneration, and probably also in retinitis pigmentosa. It may result from vascular insufficiency in arterial disease, or from senile degenerations, and, finally, it is possible that certain of the toxic amblyopias are due to poisoning of the ganglion cells in the retina, rather than to poisoning of the nerve fibres behind the bulb.

I can only here refer to one or two of these cases which are of more immediate neurological interest.

Retinitis pigmentosa is a familial disease not infrequently associated with a familial form of inner ear or nerve deafness, and occasionally associated with a family history of epilepsy. It is apt more especially to occur in the offspring of consanguineous marriages. It belongs to the class of diseases which Gowers has in a cynical mood called "abiotrophies"—system degenerations whose cause and nature are unknown.

The close relationship of amaurotic family idiocy and cerebromacular degeneration has been sufficiently proved in recent years. In both there is a lipoid degeneration of the ganglion cells in the retina, as well as in corresponding cells in other parts of the central nervous system, especially in the cerebral and cerebellar cortex. The infantile form is intense in its development and fairly rapid in its course, the infants rarely reaching the age of two years. The juvenile form, as a rule, commences during second teething or towards the end of that period, and between that and puberty. It is less intense in its action and slower in its course, the unfortunate children sometimes living to the age of sixteen or seventeen years. I believe, however, that a very much milder form, or a closely allied disease, may manifest itself at puberty, or shortly thereafter, in which the macular disease is manifest and very slowly progressive, but in which the cerebral signs are only very slightly in evidence. I have in my mind a small series of cases showing macular changes and consequent optic atrophy, clinically indistinguishable, so far as the retinal appearances are concerned, from cerebromacular disease, but in which the main—if not the only—evidence of any cerebral affection is a marked change in disposition and loss of mental control.

The further discussion of this group of cases would lead us too far into a discussion of retinal disease in general. As a rule, the ophthalmoscopic examination

is sufficient to establish the diagnosis, but every now and again cases occur in which it is not easy to decide whether we have to deal with a primary or secondary retinal atrophy, and in such cases the visual fields may prove of value in helping to a decision.

Group 2.—Papillary Atrophies.

In the second group of cases, the initial damage to the nerve fibres takes place at the disc itself. In this group are the atrophies due to glaucoma, those following on papillitis and papillœdema and a rarer group in which a cavernous degeneration in the disc tissues occurs in high myopes. To complete the grouping there should also be included the very rare occurrence of traumatic avulsion of the optic nerve.

The atrophy that occurs in papillœdema has two main causes. In the early stages, the nerve fibres themselves are unaffected, apart from the disturbance in their course produced by the swelling and displacement of the fibres, and there is no functional loss, if we except a slight enlargement of the blind spot from mechanical displacement of the retina. But as time goes on, the nerve fibres lying in the œdematous fluid begin to swell up and show moniliform varicosities. The swelling is in the cement substance binding together the individual fibrillæ which compose the nerve fibres. These disintegrate as the swelling increases and the whole fibre degenerates into fatty débris. In the third stage, an increasing neuroglial proliferation in the disc replaces the degenerate fibres and as it contracts down, it squeezes and kills out the nerve fibres left intact. At the same time, an endothelial proliferation obliterates the channels of the smaller vessels and the final condition is an opaque white disc of neuroglial tissue filling the position of the optic disc.

In a papillitis the proliferative process affects also, or, at least, to a greater degree, the mesoblastic tissues round the vessels at the entrance to the disc, and after subsidence of milder degrees of this condition, where there has been considerable restoration of function, the disc may seem as if covered with a connective tissue film. I have at present under observation a particularly good example of this type of result in papillitis, where the only permanent functional loss affects a small segment in the lower field, and the disc shows this appearance of connective tissue film over it and following some distance out along the lines of the principal vessels.

Incidentally I may note that the occurrence of white lines along the vessels in the neighbourhood of the disc is not in any way an essential feature of the atrophy following papillœdema. The arteries are always constricted, but often do not show white lines.

In glaucoma the nerve fibres are mainly destroyed at the disc as the result of the increased intra-ocular pressure. The lamina cribrosa yields under pressure and recedes, and the nerve fibre bundles are stretched over the unyielding edge of the sclera and atrophy.

Enough has been written on the nature of the field defects in glaucoma to enable this condition of optic atrophy to be easily diagnosed, though there is a small number of cases in which an atrophy associated with arteriosclerosis gives rise to doubt. In the cavernous degeneration of Schnabel, the optic disc shows the same form of cupping as in glaucoma, but its occurrence in high myopes, without raised intra-ocular pressure, and the difference of the fields, sometimes reduced to a tiny central area, should excite suspicion.

Group 3.—Atrophy due to Retrobulbar Lesions.

This is the largest group of cases and is subdivided into: (*a*) Orbital; (*b*) Foraminal; and (*c*) Intracranial lesions. Though some of the inflammations may occur in any part of the nerve, or may affect the whole nerve from the chiasma to the bulb, papillitis, indeed, is only an optic neuritis in which the anterior part of the

nerve, after the entry of the blood-vessels, is affected. Wilbrand and Saenger, in talking of the forms of neuritis which give rise to optic atrophy, use the terms "acute" and "chronic," "peripheral" and "axial neuritis." I prefer to speak of interstitial and parenchymatous forms.

An inflammation may attack the parenchyma of the nerve directly, or it may invade the nerve from the periphery through its meningeal coverings and its interstitial fibrous structure. It may be the result of any form of meningitis, acute or chronic, septic, tuberculous, or syphilitic, and the resulting atrophy may be complete or partial. It may result from orbital inflammations, and these may be the result of sinus inflammations, or infection from dental abscesses.

Probably the commonest form of parenchymatous inflammation is associated with disseminated sclerosis. I am afraid I am not prepared to follow some of my colleagues in ascribing 99% of all cases of acute retrobulbar neuritis to disseminated sclerosis. There are so many other causes of acute myelitis of the optic nerve which give rise to an optic atrophy. I have records of cases of post-influenzal myelitis, of syphilitic myelitis, of atrophy following Malta fever and blackwater fever, of post-herpetic neuritis, of post-varicellar neuritis, most of these seemingly of the acute parenchymatous type and all giving rise to optic atrophy. These are only a few of the cases that come to my mind while writing.

I would like to refer, for a moment, to one of these forms, the optic atrophy occurring during ophthalmic herpes. Though described originally in 1866 by Jonathan Hutchinson, the occurrence of this complication of herpes zoster ophthalmicus seems to have attracted very little attention. In a paper I published some years ago on "Ocular Lesions of the Trigeminal Nerve" I described some cases of it and referred to a number of others. I confess that I can throw no light on the pathogenesis of the optic atrophy in these cases. During the acute stages of the herpes, the eye is not in a condition to allow of proper fundus examination, so the cases are not usually seen until the atrophy is obvious. I believe that there may be an acute œdema in the distribution of the nervi nervorum arising from the 5th and supplying the optic nerve sheath, and that this affects the nerve. I do not think it is probable that the inflammation can have spread from the Gasserian ganglion to the intracranial portion of the nerve. As, however, I know of no autopsy on such a case I cannot speak with any authority on the cause of the atrophy.

Among the other lesions acting on the orbital portion of the nerve must be recorded tumours. These may be intraneural or extraneural. Some years ago, I showed two cases at a meeting of the Section: one of an intraneural tumour causing intense papillœdema, the other of an extraneural tumour causing optic atrophy. The apex of the orbit is not an infrequent position for a gumma to develop, and this may be a cause of pressure on the nerve.

Foraminal lesions.—Lesions acting at the optic foramen form an interesting group of cases giving rise to optic atrophy. The first and most frequent cause acting here is trauma. The trauma need not imply a fracture passing through the optic foramen. Indeed, in quite a number of cases, even where there is a basal fracture, the optic foramen is not involved in it. But there is a closer attachment of the nerve sheath coverings to one another at the optic foramen and the nerve sheath itself is here bound down to the bony wall. There is also a freer interchange of blood-vessels at this point and these get torn through readily in skull injuries and give rise to sheath hæmorrhages and nerve tears and consequent atrophies. Many of these cases show very interesting segmental losses in the visual fields.

It is a matter of dispute as to whether the optic atrophy occurring in oxycephaly is a result of the narrowing of the optic foramen, or whether the optic atrophy and the skull deformity may not both be coincidental results of an early meningitis. In the case of Paget's disease, however, I think there is little doubt that the bony thickening reducing the calibre of the optic foramen is the cause of the atrophy.

My attention was first called to this cause of optic atrophy many years ago by its occurrence in a typical case of leontiasis ossea. Since then I have seen five cases of osteitis deformans with optic atrophy. Two of these cases have already been shown at meetings of the Section. They are very slowly progressive in their nature and show curious irregular losses in the visual fields, partial ring scotomata and paracentral scotomata, with irregular peripheral contraction of the fields. In time, the visual loss becomes complete. In nearly all these cases, there is evidence of pressure on other nerves, especially the auditory and the trigeminal. Indeed, we had to operate on the case of leontiasis ossea to try to relieve the intractable neuralgia.

Sclerotic changes in the ophthalmic artery as it passes through the optic foramen may also be a cause of optic atrophy. If you look at the base of the skull after removing the brain, you will see what a sharp edge the dura makes as it roofs over the intracranial entrance to the optic foramen, and coming close up to the outer side of this is the convex curve of the internal carotid artery which gives off, almost as it touches the optic nerve, the ophthalmic artery. The consequence of this anatomical arrangement is that any sclerotic changes in the walls of either the internal carotid or its ophthalmic branch causes pressure on the nerve at a point where it cannot yield, and, in consequence, it atrophies. A series of pictures in Vol. III of Wilbrand and Saenger's "Neurologie des Auges" illustrates this form of atrophy most beautifully.

Intracranial portion of the nerve.—Among the atrophies arising from causes acting intracranially, we have to deal with quite a different set of factors. Disseminated sclerosis, of course, must still be regarded as an important cause and the patch may be, and often is, found to affect the chiasma and both nerves. Meningitis may still be a cause, but of course it is to be remembered that in many of the acuter cases death occurs while the inflammatory stage is still present and before any sign of atrophy is manifest. Meningitis also may cause a pressure atrophy by blocking the foramina leading from the ventricles to the cisterna and setting up an internal hydrocephalus. The main intracranial form of atrophy is the pressure atrophy caused by growths, especially in the pituitary and suprapituitary regions, or on the base of the frontal lobe or anterior end of the temporo-sphenoidal lobe.

I called attention many years ago to the importance, from a localizing point of view, of the appearance of an atrophy on one side and a papillœdema on the other side. Almost the last lecture that Sir William Gowers gave at Queen Square was devoted to a case of this kind of which I had cut the sections. Subsequently Kennedy gathered together several cases illustrative of the value of this phenomenon as indicating the location of the pressure.

I am afraid, however, we use the word "pressure" in a loose way. Many writers have drawn attention to the probability that the atrophy in pituitary cases in many ways is more likely to be the result of a stretching than of a pressure and the beautiful work of Schüller and the Vienna school of radiologists has brought this out more fully. The anatomical work of Schaeffer, on which de Schweinitz based much of his Bowman Lecture, showed how rarely the chiasma came into any relationship with the bony chiasmal sulcus and how little likely was the chance of its being pressed between a growth and the bone. At present, we may hedge a little and talk of a pressure traction injury to the nerve.

Basal aneurysms as well as the sclerotic changes in the internal carotids already referred to are sources of atrophy acting at the origin of the nerves from the chiasma. Much, however, has been written on this subject in recent years, and as my purpose is only to outline a scheme for the classification of the optic atrophies I must not enter into further details but pass on to consider the fourth class in which the optic atrophy results from causes of a general toxic nature not acting at any one particular focus, or where the origin is unknown. Among the toxic causes are tobacco, arsenic, lead, methyl alcohol, carbon bisulphide, quinine, *Aspidium filix mas* and others.

The action of these varies, and some seem capable of acting in more ways than one to produce atrophy. It is still an unsettled question whether tobacco primarily poisons the ganglion cells in the retina or the nerve fibres behind the bulb, and the same doubt exists as to methyl alcohol and carbon bisulphide. Quinine and *Aspidium filix mas* act by producing retinal arterial spasm and consequent retinal atrophy. Arsenic seems to act directly on the nerve fibres. Lead may seemingly act either directly on the nerve fibres or indirectly by causing arterial degenerations. Diabetes, the anæmias, both the toxic forms and that due to loss of blood, may cause optic atrophy. Of Leber's familial atrophy we can only say that we do not know what the cause of the lesion is. Its occurrence during the period of most active sexual life would seem to give some support to the suggestion of Fisher that it is due to some pituitary disturbance.

In this class also must be placed the optic atrophies that occur in association with other systemic degenerations in the central nervous system, for example, Friedreich's disease, peroneal atrophy and hereditary cerebellar atrophy. I have already insisted on the fact that the optic nerve is not a nerve but an integral white tract of the central nervous system, and as such is liable to participate in the diseases that attack the white matter, and these degenerations are only further examples of this tendency.

I have left to the last the question of tabetic atrophy and its classification. Into which division can this most important form of optic atrophy be fitted most conveniently? This has been one of the most disputed subjects of the many disputed subjects in connection with tabes. If I may quote from a paper which I wrote upon it some eight years ago: "Various and discordant as are the theories advanced to explain the pathology of the changes in the posterior roots and columns, we find that the theories of optic atrophy are just as diverse. The possibilities may be briefly grouped into:—

"(1) A primary neuronic degeneration with secondary fibrosis:—

(*a*) Commencing in the ganglion cells (Gowers, Erb, Charcot, etc.).
(*b*) Commencing in the nerve fibres or axones (Uhthoff, etc.).

"(2) A primary peripheral and interstitial neuritis with secondary degeneration of nerve fibres.

(*a*) The primary changes commencing in the papilla (Elschnig).
(*b*) The primary changes commencing in the pial and subpial regions in the peripheral portion of the nerve (Léri, Wilbrand, and Saenger).
(*c*) The primary changes, both axial along the central vessels and peripheral in the subpial zone.
(*d*) The primary changes commencing in the optic foramen (a periostitis and pachymeningitis resulting in strangling of the nerve (Schlagenhaufer).
(*e*) The primary changes commencing in the intracranial portion of the nerve including the chiasma and optic foramen and mainly in the pial and subpial zone (Stargardt and Richter).

"(3) The interstitial changes and the parenchymatous changes in the nerve are co-ordinate results of the activity of the tabetic virus and not mutually dependent on one another."[1]

In that paper I tried to show how in its clinical history tabetic atrophy sometimes gave evidence that its primary mode of attack is interstitial and at other times parenchymatous and how in this respect it sometimes allies itself more closely to tabes and at other times to general paralysis. I have seen little cause to modify the opinion I then expressed. We find two quite definite types of history. In one, the onset is slow; fairly good central visual acuity is maintained over a long period and the segmental losses in the peripheral fields are fairly sharply delimited.

[1] *Brit. Journ. Ophth.*, 1922, vi, 289.

In the second type, the loss of central visual acuity occurs fairly quickly and vision may be grossly diminished, while the peripheral fields for white are hardly affected, or, again, there may be great variability or uncertainty in the delimitation of the peripheral fields.

Many of these cases in the early stages may show a marked difference between their vision on first awakening and later in the day. As Behr has shown, dark adaptation seems to be the first function affected by tabetic atrophy and may be present before there is any sign of atrophy. Only the pathological investigation of a large series of very early tabetics and the careful correlation of the pathological findings with the clinical history will determine whether I am right in my contention that tabes can produce optic atrophy of two kinds. In one kind, the parenchymatous degeneration is predominant and in the other the interstitial proliferation is the more obvious factor.

But we have further to see whether there is any clue to the most likely position for the commencement of the lesion. As far as clinical history goes, I think it is strongly in favour of Stargardt's contention that the chiasma and intracranial portion of the nerve are first affected. The frequent symmetry of the visual fields is a strong point in favour of this hypothesis. It would take too long a time to repeat again all the arguments quoted in my original paper, but I have seen little cause since then to modify my general conclusion that tabetic atrophy in tabes is partly interstitial and partly parenchymatous and so far resembles G.P.I., and that the clinical symptoms vary as the one or other process predominates, and, finally, that as a general rule the process commences in the proximal portion of the nerve and not in the periphery or distal portion.

I have only sketched briefly and with many omissions a scheme of classification of optic atrophies. Briefly summarized—my primary divisions are founded on the site of attack of the primary lesion, and these, in turn, are subdivided on the basis of the nature of the lesion. To develop and illustrate the subject fully would take more time than even your patience, great though it is, would accord to me. In my experience a scheme such as I have outlined has proved most useful for teaching purposes and for impressing on students the manifold causes of optic atrophy. I hope, at least, to have made manifest the reasons for my strong aversion to the present use of the terms " primary " and " secondary " in the forced and misleading sense in which they have been employed for so long. And if what I have said to-night will induce any ardent worker to take up this question and try to establish a true classification of optic atrophies, I shall feel I have not spoken in vain. The ideal combination would be a neurologist and an ophthalmologist, and much pathological spade-work is necessary. The material is available if only the workers will come forward.

Section of Orthopædics.

President—Mr. P. JENNER VERRALL, F.R.C.S.

[*October* 7, 1930.]

Pre-natal Separation of the Lower Femoral Epiphysis.—P. JENNER VERRALL, F.R.C.S. (President).

A baby, 10 days old, born under competent observation in the Royal Free Hospital: a breech presentation with extended legs. No great violence was needed to bring down the legs and it is reasonably certain that the injury was not a natal one.

Clinically and skiagraphically there is a separation of the left lower femoral epiphysis forwards. Attempts at reduction have failed.

This appears to be a very unusual case and any advice as to treatment would be welcomed. The alternatives are: (1) Suspend the child by the leg, trusting to steady traction to produce a reduction. (2) Operate at once to try to replace the epiphysis, with the risk of impeding growth. (3) Allow the deformity to remain, in the expectation of performing an osteotomy later in life.

I should propose an attempt at (1) with no great hope of success, to be followed by (3) if necessary.

Discussion.—Mr. MCCRAE AITKEN said that he would advise hanging the child up by the heels and seeing what happened.

Mr. HOPE CARLTON said that he knew of a case in which an infant, aged 8 months, had a similar displacement of several weeks' standing. A splint had been applied and the child "hung up"; after three or four weeks there had been a perfect reposition.

Dr. RALPH PHILLIPS said he understood that the child was a premature one, and therefore he wondered whether the condition was a syphilitic osteo-chondritis, with separation of epiphysis. If the child were slung up with the legs straight, would there be any danger of the lower end of the shaft of the femur pressing on the popliteal vessels?

Mr. JENNER VERRALL (in reply) said the question as to the baby being syphilitic was under investigation. He would not entertain any fear with regard to the popliteal vessels as a result of simple suspension.

Absence of Right Fibula, and other Congenital Deformities.—PAUL BERNARD ROTH, F.R.C.S.

Betty C., first seen May 15, 1924, when 2 years old, with the following congenital deformities:—

(1) Absence of right fibula. (2) Intra-uterine fracture of right tibia, with severe forward bowing. (3) Left talipes equino-varus, extreme, with large callosity over outer border of foot. (4) Absence of a toe on each foot. (5) Absence of two fingers on each hand. (6) Complete fusion of the two fingers of both hands.

The first two conditions had resulted in severe valgus deformity.

Treatment.—July 1, 1924, left astragalectomy: foot over-corrected; plaster.

July 15, 1924, cuneiform osteotomy of right tibia from in front, to correct the anterior bowing; plaster.

Subsequently the right leg was fitted with a walking instrument, and has never needed any more operative treatment, but the left foot has been a constant source of worry. Between November, 1924 and January, 1928 the foot was manipulated and plaster applied on many occasions. At each manipulation the foot came reasonably straight, but it always relapsed.

The child then disappeared for two years, when she was brought to see me again through the Shaftesbury Society. She now walks fairly well, but the left foot is so varus that the weight is borne entirely on the outer side of the os calcis. Can anything be done to remedy this ?

Comment.—This case serves to show the uselessness of performing astragalectomy in an infant. If it is performed it should not be before the age of 11 or 12 years.

Discussion.—Mr. LAMING EVANS said that in 1871, Lunn, of Manchester, first removed the astragalus on one side, then on the other, in a child aged 2, and published the case six months later in the *British Medical Journal*, stating that he had obtained good correction, but Lunn never followed up and published the late results. He (the speaker) had never seen a series of cases of astragalectomy in children which had reported efficient feet at the end of five years, and he believed it was generally recognized that astragalectomy should not be performed at a younger age than 10 years. If there was going to be trouble in this child, it would be due to an arthritis of the subastragaloid joint similar to that taking place after fracture of the os calcis. In that event the subastragaloid joint should be arthrodesed.

Mr. D. MCCRAE AITKEN said that he personally did not like astragalectomy at all, if it could be avoided; he had never seen a good result from it after five years. His treatment would be the same as for congenital absence, namely, to keep the child under observation and treatment year after year until she was grown up. This meant the continuous use of plaster and the wearing of a boot, and then twisting the foot again, but if the patient was lost sight of for a year or so a deformity would ensue which would need a good deal of replacement.

Mr. ALAN H. TODD said that the child was shown in the hope that someone would suggest treatment of the condition as seen now. He thought the reason the foot came round so much was that the astragalus was absent, and it might be a help if the gap could be filled with something which would prevent telescoping. Some time ago he had had to deal with a relapsed case of ordinary talipes equino-varus. He divided the nuclei on the inner border of the foot, opened it out, and put into the centre of the nuclei some wedges of decalcified bone —which it was now difficult to procure. That was carried out a year ago, and the corrected posture had persisted. That might help in this child.

Fracture of Right Astragalus.—PAUL BERNARD ROTH, F.R.C.S.

Margaret S., aged 18, was sent to me by Dr. William O'Brien on April 3, 1930. Two days previously she had jumped off a spring board on to a thick mat in a gymnasium, and hurt her right foot.

The skiagram by Dr. Wylie showed a complete transverse fracture right through the body of the astragalus, with partial separation of the two fragments.

Treatment.—Rest in a tin night-shoe, massage and radiant heat. This last was omitted after a fortnight.

On July 22 she was allowed to walk for the first time, using crutches.

On September 25 she said that she could walk three miles without swelling or discomfort. She had attended for massage altogether forty-nine times.

She is regaining complete range of movement.

The skiagram shows bony union.

Comment.—I have shown this case because isolated fracture of the astragalus in ordinary civil life is very rare. I have seen only one other case; that was under the care of the President. In aeroplane accidents it is however very common, and has even been called "aviator's fracture." The late H. Graeme Anderson has referred to eighteen cases in his book on "Medical and Surgical Aspects of Aviation." The

reason for this frequency is that in a crash the victim comes down with the middle of his foot resting directly on a bar, and the force is transmitted directly through the middle of the astragalus. In ordinary falls from a height it is nearly always the os calcis which touches the ground first and is fractured.

The prognosis is not very good. According to Von Bergmann there is always some disability afterwards, as much as 30% on an average. In the present case I hope to get, in time, a nearly perfect recovery. Lack of dorsiflexion is the difficulty; but this is compensated for in the present case by the wearing of an ordinary high heel.

Discussion.—The PRESIDENT said that the case in his own practice to which Mr. Roth had referred was one in which there was complete displacement of a posterior fragment of the astragalus under the tendo Achillis. He replaced this portion, though with difficulty. The patient went to another hospital for massage, and the posterior piece was there found to be undergoing aseptic death. Subsequently, however, the patient recovered considerable function.

Mr. MCCRAE AITKEN said that a piece of new bone was forming on the front and that would check dorsiflexion. For that reason he would get the foot as much dorsiflexed as possible. From his experience of fractures into the calcaneo-astragaloid joint, he would keep the foot in plaster longer, but would allow the patient to walk in the plaster.

Mr. B. WHITCHURCH HOWELL said that the foot was pronated and stiff, chiefly in inversion; it was impossible to invert it without causing pain. He regarded that difficulty as more important than the slight limitation in dorsiflexion. Without treatment the patient would become more flat-footed and stiffer and would have more pain.

Mr. ALAN H. TODD said that he had frequently seen fracture of the astragalus, and he thought that, even when there was subastragaloid arthritis, the disability was not so great as with a fracture of the os calcis. He would not arthrodese this patient's joint, at least until she had a disabling arthritis. He had a patient now, aged 24, with advanced arthritis, as shown by the skiagram, but there was surprisingly good function.

Mr. HOPE CARLTON said that when the fracture was of long standing and involved the ankle-joint, with a good deal of disability, an excellent result followed astragalectomy. When the fracture involved only the subastragaloid surface he had seen a good result follow the Dunn operation.

Compression Fracture of Sixth Cervical Vertebra.—C. HOPE CARLTON, M.C., M.Ch.

W. H. J., male, aged 20.

April, 1930.—Dived into 2 feet of water from a height of 30 ft. Fell on his head and was conveyed to hospital; did not lose consciousness. Was kept three days in Puento Arenes, Costa Rica, and was then returned as passenger to this country, and did light work on board ship.

August, 1930.—Complains of: (1) No grip in hands, aching pain along ulnar border of fore-arms. (2) Pain in neck on coughing.

There is no sensory disturbance. Limbs symmetrical in shape and size, almost full movements of head and neck. Slight symmetrical wasting of interossei. Knee-jerks exaggerated. Babinski, negative.

Electrical Reactions.—All present but markedly weakened.

Report of X-ray Examination.—Compression fracture of body of sixth cervical vertebra, with angulation of canal.

August 8, 1930.—Minerva jacket applied. August 19.—Still some pain in arms. August 29.—New jacket applied. More power in hands and pain somewhat less.

October 7.—Continued increase in power of hands. New jacket applied.

Discussion.—Mr. ROCYN JONES said that as the patient was comfortable he would not be disposed to manipulate the neck, but would give him a collar for six months. During the last eighteen months he (the speaker) had had two patients with similar symptoms, but there was little to be seen in the skiagram. One was a boy who had pitched on to his head when diving

When he came out of the water his arms were paralysed and remained so for two days, and they were extremely painful. He recovered completely. The other was a man who pitched off a scaffold and was fortunate in escaping fracture; he had a hæmorrhage into the spinal canal and a patchy paralysis in the upper limbs. He also recovered completely, and returned to his work.

Mr. B. WHITCHURCH HOWELL said that he was against manipulation of the spine in such cases. A case had occurred in the practice of a colleague, in which paralysis of the diaphragm had followed the procedure.

Injury to Brachial Plexus.—W. H. OGILVIE, M.Ch.

E. M., a girl, aged 12.

History.—Motor accident two years ago, resulting in injury of the left brachial plexus. No fracture of humerus or clavicle. The paralysis seems to have been complete, involving all muscles supplied by the plexus. A year after the accident there was no recovery of any kind. The case was taken to Court, and the patient was awarded £1,500 compensation. At this time she was shown at a meeting of one of the Sections of this Society, and amputation was advised by all the surgeons who discussed the case.

Present Condition (one year later).—There has been a remarkable recovery of muscles at all levels in the arm. The only groups in which there now appears to be no power are the external rotators of the shoulder, the rotators of the forearm, the extensors of the wrist, and the extensors of the last two joints of the fingers. These groups are supplied from different levels of the brachial plexus, in each of which levels muscles supplied from the same roots are acting. It therefore appears likely that there is no complete anatomical lesion, and that many of the muscles which now show no power may recover when the contractures are overcome, and the paralysed muscles relaxed.

The case is shown to emphasize essential lessons of lesions of the brachial plexus: that they nearly all recover to a surprising extent, but take very long to do so, and that operation is rarely indicated in the early stages.

Mr. MCCRAE AITKEN said it was important to know the mechanism of the accident, i.e., whether the patient was "brushed" by the side of a car. He had been contemplating sending to the medical journals an article on the danger of motor-car accessories, because within two years he had had three cases of severe brachial plexus injury. In one case total loss of power in the arm had followed, and on the advice of a neurologist amputation was performed. In the second case there was a patchy recovery, such as Mr. Ogilvie had described. In the third case the "law's delay" caused nothing to be done for some time, and then, as a result of a strong letter from himself (the speaker), the case was brought into hospital, and recovery ensued. Recently there had been almost universally introduced on motor cars an accessory which projected beyond the edge, and was very liable to cause injury, especially to persons cycling and wobbling a little. There was no need for these accessory parts to project; it was quite easy to make them counter-sunk. They were also placed on the bonnets of cars; he had seen one, in the form of a bird, which projected 5 in.

Congenital Abnormalities of the Hands.—W. H. OGILVIE, M.Ch.

F. B., a girl, aged 10, came to hospital last week complaining of pain in the right hip. Her parents state that she has had this pain for a month and has been limping very badly. She walks with a very marked limp, holding the right hip and knee flexed and the foot in a position of equinus and valgus. On examination, there is no wasting of the muscles of the thigh or calf. Passive movements of hip, knee, and ankle-joints are full and free. No abnormality can be seen or felt in either hip or knee, and skiagrams of both hip-joints show no evidence of disease.

I am inclined to look on this as a hysterical limp. The limp is almost too good

to be true, and there is no objective sign of disease. I feel, however, afraid of diagnosing hysteria at the age of ten.

Much more interesting, from the orthopædic point of view, is the condition of the two hands, in which the thumb is replaced by an additional finger. This outer digit is separated from the others by a web which is only slightly broader than that between the fingers. There are three phalanges, and there is no thenar eminence.

Muscle Test.—The extensor of the thumb arises with the extensor communis

Congenital abnormalities of hands: right hand and wrist-joint.
(Skiagram by Dr. H. C. Courtney Gage.)

digitorum. There is no trace of an abductor pollicis or of separate extensors of the thumb. Sometimes there is a suspicion of what might be a flexor brevis, but it is very difficult to say.

Skiagrams.—Each "thumb" has three phalanges; the middle phalanx on the right thumb has no epiphysis. The metacarpal has an epiphysis at each end, thus having the characters both of a finger and a thumb metacarpal. There does not appear to be any abnormality in the carpal bones.

Discussion.—Mr. P. B. ROTH said he would ask, What was a thumb? He thought this child had thumbs, which happened to have an extra phalanx, and that was why they looked so peculiar. He did not agree with Mr. Ogilvie that no small muscles of the thumb were present. If that was the case, how could opposition be possible? Yet opposition was made with the little finger. The flexor brevis was also present.

Mr. OGILVIE, in reply to Mr. Roth, said that the digit in question was the same in diameter as a finger, the angle at which it was set was the same, it had the phalanges and the metacarpal of a finger, the long muscles were those of a finger, not of a thumb, and it had an opponens. The presence of the flexor brevis was somewhat doubtful. Nine out of ten features pointed to the digit's being a finger, not a thumb.

? Bipartite Scaphoids.—W. H. OGILVIE, M.Ch.

F. M., male, aged 32. Sustained minor injury to right wrist in spring, 1930. Afterwards the wrist caused him occasional pain. A skiagram was taken and the report returned was "fractured scaphoid." Excision of the proximal fragment was recommended; but a skiagram of the other wrist showed an identical condition.

FIG. 1.—Bipartite scaphoids: right (injured) wrist.

The radiographic appearance is identical in both wrists (see figs. 1 and 2). The line of "fracture" is much nearer the proximal end of the bone than usual, and the two fragments have smooth surfaces, suggesting they are truly articular and not due to a false joint. Are these fractures, or do they mean a persistence of the os centrale? Whatever the ætiology, is operation advisable?

Some additional trauma appears to have occurred on the right side where there is a detached fragment at the tuberosity of the scaphoid, and the proximal bone seems to project dorsally to an abnormal extent.

FIG. 2.—Bipartite scaphoids: left wrist.

Discussion.—Mr. B. WHITCHURCH HOWELL said that this patient had loss of function, with pain during his work, and found it difficult to crank an engine (his work was dismantling motor-car engines). He thought this justified removal of the scaphoid on the affected side. There was radiological evidence on both sides, but the pathological disability was on the right side only.

Mr. MCCRAE AITKEN said he believed that there was an arthritis between these two fragments, due to a jar. He would rest the wrist on a small cock-up splint; in six months' time there would be comfortable movement. He deprecated removal of any part of the scaphoid in this patient.

Mr. S. T. IRWIN said that three or four years ago, at a meeting of the British Medical Association, he looked up fifty consecutive cases of fracture of the carpal bones, and one of these seemed to be a case of neat fracture of the scaphoid, yet the patient had recovered good function of the wrist. Therefore it was decided to have a skiagram of the other side, and that was found to be the same; one side was just a replica of the other.

Tuberculous Knee with Unusual Skiagraphic Appearance.—HAROLD EDWARDS, M.S.

Patient, female, aged 30.

Twelve years ago the left knee became painful and prevented walking. After

two weeks the knee recovered sufficiently to permit walking, though it has been slightly painful ever since.

During last few months pain has increased considerably and joint has become swollen.

On Admission (King's College Hospital): Considerable effusion in left knee and synovial membrane appeared to be thickened. A swelling also noted behind joint. Thigh muscles wasted; movement painful. Complete extension not quite possible; flexion limited to right angle. Fine crepitus noted on movement. Patient has a congenital subluxation of right hip.

FIG. 1.—Note lipping, and "honeycombing" of the lower end of the femur.
(Mr. Harold Edwards's case.)

Skiagrams (figs. 1 and 2) show considerable lipping of articular margins of joint and a honeycombed appearance of bone at lower end of femur. Blood Wassermann reaction negative.

The joint was opened through a small incision to the outer side of the patella, and a small portion of the synovial membrane removed for microscopical examination. A large quantity of slightly turbid amber-coloured fluid escaped when joint was opened.

Pathological Report.—(1) A few colonies of *Staphylococcus albus* were cultured. (2) A section of the synovial membrane showed typical tuberculous granulation tissue.

FIG. 2.—Note the destruction of bone at the posterior aspect of the femur.

Discussion.—Mr. MCCRAE AITKEN said that this patient had had pain for twelve years, therefore something should be done for the knee. Whatever the infection, it was surprising that more damage had not occurred during so long a time. If necessary he would advise an exposure of the knee by splitting the patella; he had carried out this procedure in cases of doubtfully tuberculous knees; it gave a fine access. Or he would perform a simple arthrodesis. One could then discuss the balance of the other limb and see whether it was advisable to operate. In some cases of subluxated hip the patients walked without pain throughout life, and one limb's being shorter than the other was not a disability.

Mr. ASLETT BALDWIN said he would suggest sending the patient to Switzerland for Dr. Rollier's sunlight treatment.

Mr. EDWARDS (in reply) said his own view was that any operative action on that limb should be amputation. The destruction of the femur was an inch above the articular cartilage. Apart from that, he did not regard the patient as a fit subject for excision of the knee. Behind the popliteal space she had a soft swelling, probably a cold abscess. He was inclined to postpone amputation for six months and see what happened.

Section of Ophthalmology.

President—Mr. ELMORE W. BREWERTON, F.R.C.S

[*October* 10, 1930.]

PRESIDENT'S ADDRESS.

Entoptic Phenomena.

By ELMORE W. BREWERTON, F.R.C.S.

THE subject I have chosen for my paper is very fascinating, as we can see most of the phenomena in our own eyes. We are often asked by our patients to explain various phenomena due to shadows thrown on to the retina, and we ought to be familiar with them and the methods of demonstrating them, and they should also be explained to medical students.

By entoptic phenomena are meant the subjective observations of objects within the eyeball. They are shadows thrown on to the retina by objects in the transparent media of the eye, of a different refractive index from that of the medium in which they lie.

It is not necessary that they should be opaque in order to throw shadows. If they are not opaque those with a higher refractive index will appear luminous, with a dark border, and those with a lower index than that of the medium in which they lie, will have a dark centre and luminous edges.

They may come from the cornea, the lens, the vitreous, or the retina.

Before the advent of the ophthalmoscope they were considered to be of very great importance. Brewster, Mackenzie, Listing, Donders, Yago, and Tscherning wrote on this subject, and in volume xxxviii of the *Transactions of the Ophthalmological Society* Sir William Barrett described an instrument which he had invented and patented in 1905 for the observation of these shadows, and which he called a "New Entoptiscope."

There are many methods of demonstrating these shadows: By looking at (1) the bright sky, (2) the illuminated field of a microscope, (3) a bright reflected bead of light, (4) an artificial light with the lids nearly closed, (5) the sky or a light through a minute pinhole. Lastly, the retinal vessels throw shadows if a light enters the eye through the sclerotic. Shadows from the cornea, lens, and vitreous can be seen together by all these methods except the last, but some methods show the lens shadows better and others the vitreous shadows.

The shadows that come from the cornea are not really "entoptic," as they do not originate in the eyeball, but as they must be considered, I propose to deal with these later.

The Lens.—The shadows from the lens are best seen by looking at a light through a minute needle-hole $\frac{1}{10}$ of a millimetre in diameter, or even less; in fact the hole can hardly be too small. It should be so minute that when looking through it nothing can be seen unless it is directed to a bright light, and then only the beam of light. In its simplest form it can be made by pricking a piece of dark paper with the point of a very fine needle. The paper should then be held in front of a bright light at about 5 in. from the eye. No correction for errors of refraction or presbyopia is necessary. If the hole is too large, a much improved view of the lens shadows can be obtained if a − 20 or − 40 lens is held between the eye and the hole. The apparent size of the illuminated area which is seen is dependent on the size of the observer's pupil, and does not vary if the hole is $\frac{1}{5}$ of a millimetre or a full millimetre in diameter. It can be seen to contract and enlarge on covering and exposing the other eye to the source of the illumination. This can be shown best by

pricking two minute holes about 3 mm. apart. Two illuminated areas are then seen which just touch each other. On covering and uncovering the other eye they can be seen to touch and separate.

The edge of the illuminated area shows innumerable bright projections extending outwards for a very short distance. These are seen only if the hole is sufficiently minute. They are probably an optical effect, and have nothing to do with the eye.

It is astonishing what clear-cut details can be seen in this illuminated area.

Any true opacities, such as striæ or dots in the lens, if they invade the pupillary area, will appear dark, but transparent striæ, congenital dots, and the physiological lens sector lines will appear bright with dark borders as their refractive indices are higher than that of the rest of the lens.

A practical point here arises: if the observer has any true defect in the pupillary area of his lens, the mirrors of his ophthalmoscopes will suit him better if he has a rather larger central opening in them than usual.

The Vitreous.—Most of our trouble with patients who complain of entoptic shadows arises from shadows thrown by strands in the vitreous.

Patients often complain of the sudden appearance of these. It is possible that the shadows are old and that their discovery is accidental; but a sensible patient can usually be relied upon and we must conclude that something has happened to the eye, particularly if the floating spots were preceded by flashes of light.

It is surprising how little noticed are gross vitreous opacities. They cause blurred vision which comes and goes, but the opacities are not focused as sharply defined strands, whereas the so-called "muscæ volitantes" appear as bright, beaded, curly bands, dark against the sky and semi-transparent against a bright light.

The best method of demonstrating these clearly is to look at a bright light with the lids nearly closed. It is better to close the lids completely and then to open them slowly until a minute chink of light is seen through a bead of moisture between the lids. Most people can see many bright strands of a beaded character with dark borders, some with bright spots in them, also with dark borders. Some of these strands are large, evidently magnified by being some distance from the retina; others, which are close to the retina, are extremely small. They all appear to move more or less.

For practical purposes how are we to determine whether the shadows are pathological or physiological? With the old Morton ophthalmoscope we used to say that if the patient saw them clearly and the doctor could not, they were physiological and of no importance. With the electric ophthalmoscope and with the slit lamp and a dilated pupil much more of the stroma of the vitreous can be seen.

I think still that if the patient sees these floating strands sharply defined against the sky and the vitreous appears transparent to the observer, with an ordinary ophthalmoscope, the trouble can be disregarded.

The Retina.—In a darkened room, light focused on the sclerotic will show an inverted picture of the retinal vessels. The eye must be turned towards the nose and the light focused on the outer side, a slight continuous up-and-down movement should be given to the light. The vessels are seen clearly but only in the macular region and for about two disc diameters around the fovea. The disc itself is just out of focus. The vessels appear as dark branching streaks on a red field. It is impossible to differentiate between arteries and veins. The fovea and the vessels near it form a brilliant picture and I believe the vessels which surround the fovea could be traced more easily and accurately subjectively than by any ophthalmoscope.

Theoretically, the entoptic appearance of the macular region should be of value in an observant patient for determining early and advancing macular changes. I am still waiting for a suitable case.

One patient with a gross macular lesion in one eye saw a large black centre with vessels reaching it. The other eye was normal (I first demonstrated the normal appearance). In another case with slight macular changes in both eyes and $\frac{6}{6}$ vision in each, the patient could see no fault in the centre of the illuminated area.

If the light from a pocket lamp be directed on the closed upper lid and the eye behind the lid is directed straight at the light, a brilliant pale yellow glare is seen. If steady pressure is now applied to the eye by means of the lamp, a dark central pulsating spot comes into view, surrounded by a lighter zone: the dark spot corresponds with the systole of the heart, and lasts for a very brief part of the pulsating period. A faint reproduction of this can be seen if the eye be directed at a poorly illuminated wall or screen with the lids open and pressure applied with the finger to the outer side of the eye.

The Cornea.—Whilst examining the shadows thrown by lens striæ with a pinhole and also whilst looking at vitreous shadows with the lids nearly closed, minute bright beads can be seen which move slowly downwards and change on winking. These are minute specks or air bubbles on the corneal surface.

On winking the eyes whilst looking at a bright light some distance away, brilliant bands of light are seen at right angles to the palpebral fissure, and radiating from the source of illumination. It is interesting to analyse these. Whilst looking at the light, if the lower lid be pushed up slowly by the finger and the upper lid held out of the way, the edge of the lid as it nears the pupil is illuminated by the moisture on its margin. Just as the edge of the lid reaches the pupil, a brilliant band of light shoots upwards from the upper margin of the light. As Tscherning points out, the moisture on the lid margin acts as a prism, base downwards and bends the rays downwards.

After an upward iridectomy many patients complain of lines of light radiating downwards from any bright light. Some very sensitive patients are greatly troubled by this phenomenon. It is due to the moist margin of the upper lid bending some of the rays upwards through the coloboma. A patient with ptosis suffers in a similar manner.

Coloured rings usually originate from the cornea. They may be (1) transient due to mucus on the surface of the cornea, (2) permanent (in rare cases), (3) always present in glaucoma, if the cornea is hazy.

On several occasions when waking suddenly from deep sleep, on turning on the light, I have seen rainbow rings around the light. The rings were not very vivid; the innermost blue was quite close to the light. They did not disappear on winking the lids. I was much amused about this time to receive a visit from an oculist who had discovered the same thing in his eyes. He wanted my assurance that he was not suffering from glaucoma. He had found that the rings disappeared immediately on bathing the eyes with water. A thin film of mucus on the corneal surface is of course the explanation. In most cases of mucopurulent conjunctivitis, the patients can see the rings if they look for them.

Some people see faint coloured rings whenever they look at a light. I had one hospital patient who assured me that he had seen them as long as he could remember. I could find nothing wrong with his eyes, except slight lens changes.

The cause of the coloured rings seen in glaucoma is certainly deeper than the surface epithelium. It may come from the deeper layers of the epithelium, from the stroma of the cornea, or from Descemet's membrane.

It is interesting to note that in cases of old interstitial keratitis with permanent corneal haze, the patients do not complain of coloured rings, and in those I have examined I have failed to demonstrate them.

In spite of this I think that the hazy cornea is due to tension of the stroma fibres producing minute separation between adjacent fibres and acting like a diffraction grating. The haze instantly disappears on reducing the pressure, and cannot be due to œdema. In an eye that has been excised, corneal haze can be

made to come instantly by squeezing the eye; on relaxation of the pressure, the haze as quickly disappears. The fact that the inner blue ring is about 2 ft. in diameter at 20 ft., suggests that a different part of the cornea is involved from the epithelium. Mucus on the surface gives an inner blue ring of only about 6 in. in diameter.

My reason for bringing this subject before you is that as instruments for examining the eye become more elaborate, we are apt to neglect simple methods. I feel sure that, subjectively, much finer details can be obtained of defects in the pupillary area of the lens through a minute needle hole than an observer could make with an ophthalmoscope. The slit lamp shows so much that it is apt to be confusing.

An intelligent patient, who is aware that he is suffering from early cataract and is undergoing some treatment with the hope of the opacities becoming absorbed, can make a careful monthly drawing of what he sees and note if any change takes place. The examination, subjectively, of vitreous strands through the nearly closed lids gives a very vivid picture, but beyond that it is not of much value.

The subjective examination of a defective macular region, by means of light focused through the sclerotic, might be of value to a trained observer, particularly a medical man. Should one of us be affected either with early lens changes or macular degeneration, a record, in the form of careful drawings, taken subjectively from time to time, would be worthy of publication.

The Detection of Colour-blindness from a Practical Point of View.

By F. W. Edridge-Green, C.B.E., M.D., F.R.C.S.

(Special Examiner and Adviser to the Board of Trade on Colour-vision and Eyesight.)

Nearly all the older tests for colour-blindness were based upon some theory of colour perception. In this paper colour-blindness is considered from a purely practical point of view. All the observations are based on the facts of colour-blindness, apart from any theory, and so will hold good whatever theory be adopted.

Object of a test for colour-blindness.—Tests for colour-blindness are of two kinds, namely, those which are used for the purpose of ascertaining the special phenomena of colour-blindness and those which are employed when the inquiry is made for some practical purpose.

On account of the arrangement of signals by sea and land, it is necessary that persons employed in the marine and railway services should be able to recognize and distinguish between the standard red, green and white lights in all conditions in which they are likely to be placed.

As with visual acuity, it is necessary to fix an arbitrary standard. As we do not wish to exclude a greater number than is absolutely necessary, the object of the test should be to exclude dangerous persons and dangerous persons only.

It is not only necessary to find out whether a person is able to distinguish between the red, green and white lights, but to ascertain as well that he thoroughly understands what is meant by colour and the individual characteristics of red, green, and white respectively. Too little attention has been paid to this in constructing tests for colour-blindness. It is necessary that a sailor or engine-driver should be able to recognize a red, green, or white light, by its character of redness, greenness, or whiteness, respectively; that is to say, the examinee ought to have definite ideas of colour, and be able to reason with respect to them. All persons who are not able, through physical defect, to have definite ideas of the standard

colours and to distinguish between them, must be excluded from the marine and railway services.

An engine-driver or sailor has to name a coloured light when he sees it, not to match it. He has to say to himself: "This is a red light, therefore there is danger," and this is practically the same as if he had made the observation out loud. Therefore, from the very commencement we have colour-names introduced, and it is impossible to exclude them. Making a person name a colour is an advantage, because the colour name excludes the element of shade. If I say to a friend, "That tile is red," and he agrees with me, it is evident that one object, the colour of which is by him classed as red, is also classed as red by me. The ordinary colour-names, red, blue, yellow and green form excellent bases for classification. The engine-driver is told that red is a "danger" signal, green an "all right" signal. Therefore, it is absolutely necessary that he should know the meaning of these colour names. A test should be such as to make it impossible for the examinee to be coached through it. This is one of the most important requirements of a test for colour-blindness, and one that is rarely fulfilled. Nearly every one of the old tests failed on this account.

A test should be one which can be carried out as rapidly as is possible with absolute efficiency. Of two equally efficient tests the one which takes the least time must be selected. A test therefore should have no unnecessary details which, though of theoretical interest, are not conceived with the object in hand. The test should be made as easy and as little complicated for the examinee as possible.

Persons to be excluded.—We wish to exclude all those who are included in the following three classes: (1) Those who see three or less colours in the spectrum. (2) Those who, whilst being able to perceive a greater number of colours than three, have the red end of the spectrum shortened to a degree incompatible with their recognition of a red light at a distance of a mile. (3) Those who are unable to distinguish between the red, green and white lights at the normal distance, through defect or insensitiveness of the cerebro-retinal apparatus when the image on the retina is diminished in size.

It now remains to explain why these three classes of persons should be excluded. The first class includes the trichromic, the dichromic, and the totally colour-blind, in accordance with the facts previously stated. The trichromic never in ordinary circumstances mistake green for red, but confuse yellow with green or red. Colour is a feeble quality of objects to them, and nervousness or excitement may reduce them to the condition of the dichromic. The dichromic are liable to mistake a green light for red and vice versa.

The dichromic regard green and red as almost but not quite identical, and this fact is one which it is nearly impossible to make a person, who has not thoroughly studied colour-blindness, comprehend—either the colour-blind himself, the public, or an unqualified examiner. They find that many colour-blind persons are able to recognize different colours, and correctly name them, and therefore set down the mistakes made to want of education in colours. As a matter of fact this is exactly opposite to the reality. I have met with several dichromics who were nearly always correct when they named ordinary colours. One educated adult, in particular, had become so expert that he was often able to baffle attempts made by his friends to show that he was colour-blind. He was well aware of the fact of his being colour-blind, though, when asked the names of various coloured objects, he was nearly always correct, and did not content himself with using the ordinary colour-names, but employed such terms as cerise. This colour appears to him blue by day, yellow by gaslight.

The following will show how it is that the colour-blind are able in ordinary circumstances to distinguish between certain colours. All colours have not a similar degree of luminosity, thus, yellow is much the brightest colour. To the

dichromic, red, yellow and green have, as far as colour is concerned, a very similar appearance. They are not exactly alike in colour. Green looks a lighter and greyer colour than red. A normal-sighted person might be given a bundle of wools, consisting of three kinds; the first different tints of green, the second tints of green mixed with blue, the third shades of blue. He would be able to arrange these in groups with no mistakes.

It is very important that persons belonging to the second class should be excluded and yet none of the ordinarily used tests detect them. The rays of red at the extreme left of the spectrum are the most penetrating, as may be seen by looking at a light or the sun on a foggy day, or through several thicknesses of neutral glass. It is chiefly by these rays that we recognize a red light at a distance, and it is therefore of great importance that a sailor or engine-driver should be able to perceive them.

The third class contains persons who are able to distinguish colours easily when they are close, but fail to distinguish them at a distance owing to the nerve-fibres supplying the central portion of the retina being impaired. As a light at a distance occupies the central portion of the visual field, it is essential that the corresponding portion of the retina should be normal.

There are cases of central scotoma for colours with perfect form vision; these would, therefore, not be detected by the test for visual acuity. This class also includes those who without having a scotoma are unable to distinguish between colours at the normal distance when the image on the retina is diminished in size.

We also do not wish to exclude persons who, though partially colour-blind, have a colour perception sufficient for all practical purposes.

If the persons to be tested have to distinguish between the standard red and green lights, these lights should be used as the basis of the test: because, if any other test were used, we should still have the same problem before us, from a practical point of view. A sailor might (with reason) object to any other test, and say that because he cannot distinguish between a green and a grey wool, there is no reason why he should be unable to distinguish between the red and green lights. If other lights are used, as for instance orange, yellow-green and purple, as is the case on some railways, these must be included in the test, so that it may be shown that the examinee can distinguish between them.

It will be seen from the above that the colour-blind person names colours in accordance with his colour perception and does not guess. Though with an inexperienced examiner he may name a number of colours correctly, how different will be the case when he is examined by an examiner with a knowledge of the facts of colour-blindness! An examiner of this kind can now ask him to name colours with a certainty as to the mistakes he will make. An examination of one of each of the three chief varieties of dangerous colour-blindness will show definitely the value of colour names. A dichromic regards a certain green as white and a corresponding purple also as white. When shown these colours, why should he call them anything except the white which he sees? If the green be made yellower he will immediately call it green, if made bluer he will call it blue. Again the dichromic regards orange and a certain green as identical, therefore when asked to name an orange he will reply emphatically "green," often adding "I know that colour; it is the colour of grass." The trichromic who see yellow as red-green miscall this colour red or green. Dark yellow should be chosen, and if a red be shown first the yellow will be called green, and if a green be shown first then the yellow will be called red. Those with shortening of the red end of the spectrum may be shown a red light which they do not see at all and say so. They may be shown a pink which appears to them a definite blue, as indeed it does to a normal sighted person, when examined through a blue-green glass.

Now a colour-blind person is quite as honest as other members of the community,

and certainly does not wish to enter a profession for which he is obviously incompetent. A man who cannot see a red light at all obviously belongs to the most dangerous class of colour blindness. Yet those belonging to this class can pass most of the old tests with ease. Again and again have men of this class been examined by me with a certificate from a well-known ophthalmic surgeon stating that their colour vision was perfectly normal. A man of this kind will look at a red light at a distance of 20 ft. and declare that there is nothing there, though he may remark that he can see the hole in the lantern. He is then not annoyed at being rejected, but thankful that he has found out his defect in time.

Let us suppose that a man of this kind, though I have never met with such a case, should desire to get through the test by trickery and guessing, how is he to set about it? How can he tell when a red light is being shown him, or when there is really nothing there—the lantern can be clicked without altering the colour and the light obscured at will. How can he pick out a pink from twenty blues when all appear identical to him? The point to be emphasized specially is that there is no chance; his detection is a certainty every time. It is exactly the same with the trichromics, who are so difficult to detect by the older tests. The efficiency of the wool test is increased enormously by the use of colour names. A man is being examined, and has just passed the wool test with the greatest ease. He is now asked to pick out all the greens, and amongst those selected are several shades of orange and yellow-browns. When asked, "Why did you not put these with the test green?" he replies, "They are a different kind of green."

Colours are called pseudo-isochromatic when they are distinguished easily by normal-sighted persons, but are regarded as identical by certain classes of the colour-blind.

The pseudo-isochromatic tests in common use are those of Stilling and Ishihara and my Card Test. In order to ascertain the relative merits of these three tests, fifty consecutive referred, or appeal, cases were examined at the Board of Trade, with the following results. It should be noted that none of these cases was examined by me alone; in all of them at least three persons, and often more, were present at the examinations. In every case Captain Ellery or Captain Dowdy and the Recorder were present. Each candidate was first examined by the pseudo-isochromatic tests and the fact whether he was dangerously colour-blind or not was ascertained subsequently.

Seventeen of the fifty cases were passed and thirty-three rejected. Of the thirty-three who failed, nineteen failed with all three pseudo-isochromatic tests, but fourteen of those rejected passed Ishihara completely, and thirteen passed Stilling. Of those who were passed thirteen showed defects with my Card Test, and of those who failed all were rejected by my Card Test, in most cases failing very badly, as, for instance, not reading Card eight, a yellow-green C on an orange ground. The explanation of the difference is that a test for a dichromic will not necessarily detect a trichromic and those with shortening of the red end of the spectrum: both are obviously dangerous, as shown by the examination with the lantern and spectral tests. In my Card Test also the pattern is the same on every card, so that the examinee has to judge by colour alone and cannot follow the design of the artist.

An important point to note is that a test which is difficult to the normal-sighted is not necessarily difficult to the colour-blind. This is shown by the number of colour-blind persons who can read Stilling's plates numbers nine and ten, the reading of which is supposed to indicate very good colour perception. In fact a test may be constructed which can be read by the colour-blind, but not by the normal-sighted.

Nagel's anomaloscope is not a satisfactory test, since a man may be anomalous without being colour-blind, and 90% of the colour-blind agree with the normal equation.

Further details will be found in my book, "The Physiology of Vision," London, 1920.

Discussion.—Mr. E. W. BREWERTON (President) referring to Dr. Edridge-Green's remark that colour-blind people promptly called a colour "so-and-so," said his experience had been that these people usually hesitated before replying.

Mr. NORMAN FLEMING asked how Dr. Edridge-Green tested for amblyopia in a colour-blind person. How could he tell if a person who was colour-blind was not also suffering from tobacco amblyopia ?

Dr. EDRIDGE-GREEN, in reply to the President, said there were cases in which a man had been found to be colour-blind, and his hesitancy at a further examination was found to be due to that knowledge. There was a committee of the Ophthalmological Society on colour blindness. He brought up one engineer, who passed the wool test with the greatest ease. The late Mr. Nettleship said one could see the man was colour-blind, as he hesitated. He (Dr. Edridge-Green) then said to his friend, the late Mr. Devereaux Marshall, "We must devise some way of tackling this." He went to his Club and asked whether men there wanted to be examined. Some came up and were all normal, but all were rejected. They were hesitating each time, being very careful, whereas the colour-blind people he brought up were cocksure and went through the wool test with ease.

In answer to Mr. Fleming, as far as he (the speaker) was concerned, a man with tobacco amblyopia or ordinary colour-blindness would not be able to read the lights of the lantern, and he would be rejected. He would not be able to pass the test for visual acuity.

The report of the cases shown at this meeting will be published in the next issue of the *Proceedings* of the Section.

Section of Electro-Therapeutics.

President—Professor J. M. Woodburn Morison, M.D., F.R.C.P.E.

[*October* 17, 1930.]

PRESIDENT'S ADDRESS.

Radiology—its Progress and Future.

By J. M. Woodburn Morison, M.D., F.R.C.P.E.

I would define Radiology as "The Science and Art of Radium rays, X-rays, and other Electro-magnetic Waves": the *Science*, in so far as it reveals the laws underlying certain groups of facts;—the *Art*, inasmuch as it teaches how those laws are to be applied in practice. In its widest sense it embraces all the subjects which come up for discussion in the electro-therapeutic Section. It is so wide in its scope that already subsections are developing, and some are limiting their work to small parts of this great field. Here lies the danger of over-specialization with its limited outlook, so apt to produce the complacent satisfaction of the narrow mind.

There is in the study of radiology—that is, in the study of the electro-magnetic range of waves from the alternating current of electricity to the cosmic ray—a full and complete exercise for the finest intellects, and in their application to the relief of suffering humanity we have one of the fundamental problems in medicine. We live in an age of great and rapid progress in science. Theories have to be discarded and new ones adopted with bewildering rapidity, but it is well to remember that theories are only working hypotheses to be held lightly and abandoned whenever proved insufficient. They furnish a basis on which orderly investigation can be carried out, and as the investigation proceeds, a theory which is no longer adequate to explain and correlate the new facts discovered is replaced by another which does. The abandonment and replacement of one theory by another is an essential part in the progress of science. Just for a moment contrast the atomic theory before the discovery of X-rays and since. Dalton's atomic theory served a useful purpose, but with the discovery of new facts a new theory was essential, and so we had Rutherford's theory of the atom, providing a new basis on which to build. There is no finality in theories, and no doubt Rutherford's theory will be discarded and replaced by another when further knowledge is obtained.

The practitioner of medicine must have a scientific training—and, parenthetically, I would remark that the radiologist is a practitioner of medicine. He must seek for truth, holding his theories lightly, and must never forget that he is first and foremost a physician. I say so advisedly, for there are still some physicians and surgeons, troglodytic in their outlook, who regard the radiologist as a glorified mechanic. David Harum said that a certain number of fleas were good for a dog; they prevented

it from worrying too much about being a dog, and it may be that these people have a similar salutary effect on radiologists.

Few branches of medicine have made greater progress in the last thirty years than radiology, and we must not forget the debt we owe to the pioneers who blazed the trail. In the early days the status of the radiologist was more or less that of a photographer. In the ensuing years it steadily improved, but is it satisfactory at the present day? and what is to be its future?

The greatest obstacle to the advancement of any specialty in medicine is the opposition of the vested interests of the profession. All the special departments of medicine—ophthalmology, dermatology, otology, and even pathology—have had to fight for their position. Very little worth having is got in this world without fighting for it. These specialties and others have developed despite opposition, and are all the stronger for having had to fight.

I will pass lightly over the progress which the manufacturers have made in designing apparatus of great power and precision, and giving adequate protection to the worker. The electro-therapist is provided with new diathermy machines capable of producing the so-called "therapeutic fever," and I look, in the future, for great developments in the use of diathermy. The roentgenologist is provided with machines of such power that only experts should use them. Transformers working at 600 and 900 kilovolts have been made, and also tubes which will stand up to them, so that those who have longed for more and more penetrating rays should be satisfied. Improvement in tubes has been steady; the self-protected tube is a great advance, and does away with much heavy apparatus.

There are two things I would ask the manufacturer for in the near future, and which I think must come: the first is that all apparatus for X-ray work must be shock-proof and yet be capable of giving sufficient output for rapid work. Only those who have worked with such apparatus can appreciate the confidence and relief from fear of accidents which it gives to the worker. The second is that all X-ray films should be non-inflammable. This is essential, and the sooner we are provided with them the better for all concerned. The film industry in this country is now well established. Without doubt it has been uphill work to recover the ground lost in past years, but that has been accomplished, and the British film is now one of the best. It may be that an entirely new substance to replace celluloid will have to be produced for use as a base, but when I think of the wonders of modern chemistry this surely is a possibility! The reward will be in the safety from disasters such as have recently occurred abroad.

Radiologists are indebted to the designers and manufacturers for great improvements in the apparatus necessary for their work, and this is recognized in their happy association as members of the British Institute of Radiology.

I have paid a somewhat inadequate tribute to the genius of the designers and manufacturers of modern electro-therapeutic and X-ray apparatus, but I assure you that no one appreciates their efforts more than I do. The instruments are of such precision that almost any intelligent person can be taught to use them or supervise their working in a few weeks' time, and therein lies the danger, for there is a tendency to commercialize radiology and to forget that in the diagnosis and treatment of disease by radiological methods a knowledge of medicine and a special training in radiology are essential.

Progress in the treatment of many conditions by electro-therapeutic methods has been steady and, to mention one instance, the treatment of inflammatory conditions of the lungs by diathermy is a definite advance. Here we have a method of treatment which is only in its infancy, and which opens up a wide field for the research worker. The ultimate action of the diathermy current on tissue cells is still a problem requiring investigation.

Treatment by ultra-violet radiations is no new thing. It was said of old that there was no new thing under the sun. It has passed through the boom period and, although still suffering from the exaggerated claims made for it by some, it is now finding its place as a useful addition to the armamentarium of the physician in the treatment of many cases.

May I speak at this point of a suggestion that physiotherapy should be added to this Section? It may be that modern medicine is intolerant of certain innovations, but it is only so when the innovators set up for themselves absurd claims to be possessors of the whole truth and, repudiating all authority, hold out to those who trust them extravagant and unwarrantable expectations. The practice of medicine cannot be separated into water-tight compartments. You can never speak truly of any method of practice as being the only true one. Medicine is sufficiently catholic in its outlook to include its many and varied branches, and only those are excluded who by their own conduct shut themselves out.

With these reservations it may be that there is no objection to the inclusion in this Section of the physiotherapists. This may possibly be a question on which you will be asked to express an opinion in the near future.

In the investigation of disease by X-rays, the assurance of better methods of observation for the detection of local changes should not make us conceited, or contemptuous of those who have gone before; much of the progress is the result of their work on which it has been our privilege to build.

There is no need to put forward extravagant claims for X-rays in diagnosis; good wine needs no bush. Their use is now universal, and it is even necessary sometimes to speak of their limitations. The medical student of the present day is apt to rely too much on the X-ray examination, forgetting that it is only a part of the examination by physical means. I have always disliked the term "X-ray diagnosis." While it may be justified occasionally, it implies a limited knowledge, and surely, before a diagnosis is made, all the methods of investigation suitable for the case should be carried out and evaluated.

In X-ray treatment, progress has been made. It can now be carried out with safety both to the operator and the patient, for methods of protection have been devised which are adequate, and we have also reliable instruments for estimating dosage.

We are just recovering from the blatant and exaggerated claims which were made on the introduction of the so-called "deep therapy" to this country. I remember reading in the daily papers, immediately after the delivery of an address before this Section, of the "new cure for cancer," and it was confidently stated that 80 per cent. of cases were cured. This statement was, of course, unwarranted and untrue. It did a great harm to radiology, inasmuch as it destroyed the confidence of the public; but the public were soon enlightened, and the most healthy corrective of any innovation in medicine is an enlightened public opinion. Good resulted from it, however, in the improvement of apparatus, and it has found its true place as a method of treatment; not only of malignant disease, but of many other conditions. The term "cure" is used too loosely. We have to consider not only the cure of disease as named by custom—and how often when one is able to give a name to a disease, one ceases to investigate —but we have to consider the cure of the whole man.

In the treatment of malignant disease, I have often said that the existence of the X-ray therapy department of a hospital could be justified by the failures. If only the disease as named were considered, the treatment would be a failure, but it is different when the whole case is reviewed. Inoperable advanced cases of malignant disease are guided and cared for through a long and trying period, trying not only to the patient, but to his friends. Life is made easier and brighter, the pathway is made smooth. You may call it a failure, but viewed in another light it may be your greatest success.

At the present time radium-therapy is a highly controversial subject. There is so much loose thinking and writing about it that it is difficult to approach it with an unbiassed mind. I appreciate the excellent pioneer work of the radium institutes of London and Manchester and the work of the various research organizations in this country—work done quietly and unostentatiously and too often unrecognized. This work received due recognition in the report of the Radium Sub-Committee of Civil Research, published last year, in which the following statement appears (p. 6, para 11):—

"It is possible that the best radium practice in Great Britain is now as good as that in any country. It would, however, be a mistake on this account to conclude that in this matter Great Britain taken as a whole is ahead of, or even on a level with, all other countries. On the contrary, it must be admitted that Sweden and France hold a leading position, and have contributed more largely than has this country to the common stock of existing knowledge in regard to the treatment of cancer by radium."

I do, however, deprecate some of the recent books on this subject of "radium and cancer," the authors, being neither physicists nor radiologists and, not having the experience of the treatment of cancer by other radiations, take far too optimistic a view, create a false atmosphere, and give the public the impression that radium is a cure for cancer. It is true that they derive a measure of support from the source to which I have just referred; on p. 5, para. 9, it is written:—

"We do not doubt that, as further knowledge is obtained in regard to the possibilities of this radium-surgery, its use will develop rapidly, and in an increasing measure it will replace the use of the knife in the treatment of cancer."

The first point that I would make is that the public is intensely interested in this subject. It is an enlightened public, instructed by wireless, by the pulpit, by popular books, and more particularly by the press. It has generously provided and is generously providing the funds necessary for the purchase of radium in large quantities to be used in the treatment of cancer and for teaching and research. The medical profession cannot afford to ignore it, and the more they take the public into their confidence—telling them the truth about radium, so far as it is known to them—the better it will be, even if the disappointments are great.

It is frequently stated that cancer is increasing, and the statement has appeared in the newspapers, to the disturbance of the public. The statement is of course true in so far as the number of deaths from cancer is greater, but there is an explanation which shows that there is little cause for alarm. Dr. Dunlop, the Registrar-General for Scotland, in a recent communication to the Medico-Chirurgical Society of Edinburgh, dealt with the recorded deaths from cancer in Scotland during the period 1911 to 1928. The main conclusion from the paper is that an ageing of the population, by leading to greater numbers being alive at those ages in which the cancer death-rate is high, accounts for three-fourths of the observed increase in the cancer death-rate. With one exception—mammary cancer—the remaining increase may be attributed to better recognition of the disease principally by histological and X-ray examination; e.g., cancer of the prostate and ovary by histological methods, and cancer of the lung and intestinal tract by X-ray examination. Mammary cancer alone appears to show a true increased frequency.

This then is my second point. There is no cause for undue alarm in the increased number of deaths from cancer, but I would remark that there is no evidence from the statistics referred to that treatment by surgery of cancer has in any way affected the death-rate.

Is it not time to consider the question of making cancer a notifiable disease, so that we could have more exact information?

Radium Trust and Radium Commission.

On July 7, 1928, the Chairman of the Committee of Civil Research appointed a Sub-Committee with the following terms of reference:—

"To examine the radium requirements of Great Britain in relation to the present sources of supply and to submit recommendations."

They presented their report in March, 1929, with the result that a fund was raised by public subscription and augmented by the Government. National Radium Trustees were appointed, their duty being to hold the funds provided by Parliament or otherwise, and to purchase radium therewith and hold it for use by the Radium Commission, which body was appointed by the National Radium Trustees to deal with the custody, distribution, and use of all radium held by the trustees, having regard to the advancement of knowledge, the treatment of the sick, and economy of use; and in particular to consider and approve plans submitted to them for the use of radium for the purposes of medical treatment and research, and to make the necessary arrangements for the supply of radium for such uses. The Radium Commission, under the distinguished chairmanship of Lord Lee of Fareham, decided, after full consideration, to approach the faculties of medicine in the Universities of Great Britain asking for their assistance in carrying out these objects: firstly by nominating hospitals, which could be constituted national radium centres, and secondly by forming, along with the representatives of these hospitals, joint committees which would draw up schemes for the use of radium in treatment, teaching and research. It is, I think, the first occasion on which the faculties of medicine have been asked by a national body to assist in a national scheme, and so far the invitation has been accepted with a welcome which augurs well for the future.

This must make clear to you my third point: that the Commission does not regard the question of radium and cancer as settled, or consider that all they have to do is to dole out radium to approved institutions, but rather, that the subject is one which calls for careful inquiry and research under the guidance of the leaders of the medical profession who, by virtue of their positions as teachers and research workers, are best qualified to give a considered judgment on the value of this method of treatment.

The present position in this country as regards radium and cancer is an interesting and dangerous one.

It is always interesting to observe new fashions in medicine and to attempt the evaluation of the methods employed—even to assume the rôle of the prophet, realizing of course that "A prophet is not without honour, save in his own country, and in his own house," and to predict the outcome of it all.

It is dangerous for anyone without adequate training to attempt major surgery, and it is just as dangerous for anyone without an adequate training to use radium. Yet what is taking place at the present time? Radium centres are springing up all over the country. Young medicals who have forgotten most of the physics they learned in their first year in medicine, who have no training in radiology, who have not—solely by reason of their youth—sufficient experience of the surgical treatment of cancer to be in a position to give a considered opinion of the relative merits of radium and surgery in the treatment of cancer, are sent abroad to visit various clinics and on return are appointed radium officers to hospitals. You might think

this is an exaggeration. Let me read to you extracts from a letter written by one of the most distinguished Continental radiologists:—

"Radium therapy is not a panacea for cancer . . . it cures but a few types . . . it presents many difficulties . . . it would be wise not to make the practice of radium therapy general throughout the medical world . . . it would be better to limit it to a very small number of hospitals, perfectly equipped.

"Nevertheless, for some time past, each day on an average has brought us one of your compatriots, eager to learn. Some of them stay here a fortnight, take notes, and depart, believing in all good faith that they have grasped all we do and how we do it . . ."

My fourth point is that a thorough training in radiology is essential for those who are going to use radium, or who are to advise others regarding its use.

There are many questions which might be discussed, such as the methods of applying radium—methods which began with surface applicators, followed by the introduction of tubes into the tissues. This latter suggestion was made by Graham Bell, in a letter to Sowers of New York, in 1903. The letter reads as follows:—

Dear Dr. Sowers,—I understand from you that the Roentgen rays and the rays emitted by radium have been found to have a marked curative effect on external cancers, but that the effects upon deep-seated cancers have not thus far proved satisfactory. It has occurred to me that one reason for the unsatisfactory nature of these latter experiments arises from the fact that the rays have been applied externally, thus having to pass through healthy tissues of various depths in order to reach the cancerous matter.

The Crookes tube from which the Roentgen rays are emitted is, of course, too bulky to be admitted into the middle of a massive cancer, but there is no reason why a tiny fragment of radium sealed up in a fine glass tube should not be inserted into the very heart of a cancer, thus acting directly upon the diseased material. Would it not be worth while making experiments along this line?

(Signed) Alexander Graham Bell.

(*Published in the August number of the "American Magazine," 1903.*)

It was of course Dominici who was the first to introduce screened radium tubes into the tissues. Later on came the introduction of needles and the so-called "seeds," and lastly the radium "bomb," which must be given a trial. It is, however, a method which has so far not proved any better than the others; the dangers to those using it have been largely overcome, but the danger to the patient remains.

Finally, the wheel has gone round and we are back again to surface applicators. The trend of radium therapy in the great Continental centres is to avoid the direct introduction into the tissues of needles and tubes wherever possible, the line of advance being the development of the surface applicator designed in such a way that the distribution of tubes and needles on the outer surface will give what is for all practical purposes a uniform radiation on the skin surface. The work of Murdoch and Stahel at l'Hôpital Brugmann in Brussels is, in my opinion, a genuine advance. They have succeeded in recording the radiation given in terms of energy absorption; for after all, it is only the radiation absorbed which can be causing changes in the tissues. The methods of recording dosage in milligramme-hours, or micro-curies destroyed, is inadequate except when all other factors, such as distance, filtration, etc., are given. Murdoch and Stahel now record the dosage in the number of ergs absorbed per cubic centimetre of tissue—ergs/cms^3.

It is still a moot point whether the biological changes are in direct proportion to the energy absorption, but the determination of the latter is the rational mode of estimating radium dosage.

One bright spot in radium treatment of cancer is in cancer of the cervix. The results obtained justify its use and justify further research, both clinical and experimental.

It must, I think, be admitted that radium therapy as regards cancer is still in the experimental stage. The constant endeavour to devise new methods of using radium is evidence that the old methods are not doing all that could be desired of them. All the time, both in radium and X-ray therapy, there is a call for more powerful weapons, but these weapons are dangerous and difficult to control. It is by no means proven that the results obtained are any better; on the contrary, many of them are worse than those obtained by older methods. It cannot be gainsaid that patients sometimes die as the direct result of radium therapy, but of course this applies to other methods of treatment.

Much of the so-called radium therapy is a combination of radium and surgery, as for example, Neumann's method of treating cancer of the rectum. In many other cases radium and X-rays are combined. The practice of radium therapy still requires the co-operation of the surgeon, the physicist, and the radiologist. Radium therapy has not yet "replaced the use of the knife in the treatment of cancer." It may never do so, but it is a useful auxiliary, capable of alleviating distressing symptoms and of prolonging life.

The whole subject is one for carefully directed inquiry and research controlled by the faculties of medicine of the great universities of this country.

Before I finish, there is one aspect of the progress and future of radiology on which I must speak, even if it is only a few words. The teaching of radiology is a subject in which many of us are intensely interested. The granting of a Diploma in Radiology by Cambridge University some years ago was the beginning of a great advance, followed by Liverpool, and at a later date by Edinburgh. The young medical who wishes to specialize in this branch of medicine has now the opportunity of an adequate training and, if he is successful in passing the necessary examinations, of receiving the hall-mark of the radiologist when the diploma is awarded him.

The benefit is not only to those who are taught, it is just as great to those who are privileged to teach. At the present day, when the medical curriculum is so overcrowded that there is hardly time given for the undergraduate to think of anything but examinations, it is difficult to see how radiology can be satisfactorily included, yet, if in any teaching hospital a course in radiology is given, students will attend. I have successfully given such a course on Saturday mornings at 9 a.m., which was voluntarily attended by large numbers of students who were preparing for their final examinations. I believe they enjoyed it all the more because there was no compulsion, because it was informal, and because they found it helpful to them in the examinations. It can be made a very pleasant way of revising quite a large amount of medicine and surgery. I think the post-graduate teaching of radiology in this country is better than in any other, and although undergraduate teaching is not as yet on a satisfactory basis, it will become so in time.

Finally, I would speak of the status of the radiologist. In this country it is in many cases far from satisfactory. He is in charge of one of the most important sections of hospital work, but often without full authority. He is expected to treat cases, but is not given charge of beds, and too often is not considered to be on an equality with other members of the staff. Is radiology to remain in voluntary bondage to the vested interests?

It may be presumptuous to anticipate the future, but I look forward to the day —and I think it is coming soon—when every radiologist who has cases to treat will have charge of beds in the hospital. For the benefit of the patient and for the true advancement of radiology this is a necessity. It is only at the bedside that many things become plain, and it is by accurate daily observation of cases under treatment

that new facts are discovered leading to true advancement. Opposition we must expect, especially from those who dwell in the backwaters of medicine. They have to be suffered but there is no need to suffer them gladly. On the other hand, the leaders of the medical profession have at all times welcomed advances in radiology, and on many occasions have stretched forth a helping hand. Quite recently I had a letter from one of the most distinguished physicians of the present day, who had just returned from a visit to many hospitals and medical centres abroad. He was impressed by the extreme efficiency of the radiological departments and says without hesitation that, with certain exceptions, Great Britain is behind France, Germany, Holland, Denmark, Sweden and America, in radiology. He stresses the importance of radiology in medicine and surgery, and contrasts the status of the radiologist abroad with that accorded him here. It is gratifying to relate that his considered opinion now is that the radiologist is entitled to take his place with the physician and surgeon on terms of equality. This is what we are striving for.

There is an old French proverb: "Tout vient à point à qui sait attendre." It is often wrongly translated: "Everything comes to him who waits," instead of "to him who knows how to wait"; and so it is that in our waiting we must prepare ourselves by undergoing the training and acquiring the experience necessary to fit us for the office, remembering that if the man does not dignify the office, the office will not dignify the man.

I look forward, then, to the time when all apparatus will be shock-proof and more or less standardized so as to reduce costs, which at the present time are so great that they constitute a serious problem, not only for hospitals, but for the radiologist in private practice; to the establishment of radiological institutes in association with all teaching hospitals, in which the physicist and radiologist will work together and in which research work will be carried out; to the development of the teaching of radiology, not only to post-graduates but to undergraduates, bearing in mind its close relationship with applied physiology, anatomy and pathology.

There are some who think we have reached the end of our progress, and that there is little or nothing remaining to be done in the future. I am an inveterate optimist and think we have only touched the fringe of this great subject. The future of radiology is a bright one. Dealing as it does with the fundamentals of the universe, it calls for the best in all of us, and "the best is yet to be."

Clinical Section.

[*October* 10, 1930.]

Congenital Coxa Vara.—CECIL P. G. WAKELEY, F.R.C.S.

Eric A., aged 2 years and 2 months. Shown at a meeting of this Section a year ago.[1] There was some difference of opinion as to what the condition actually was. It is now clear that this is a case of congenital coxa vara.

Skiagram reveals centre of ossification in head of femur which is in the acetabulum. Upper end of shaft of femur is definitely bowed. Three and a half inches shortening of left femur. Child can walk well on toes of left foot and tilts pelvis down in so doing.

Different methods of treatment were suggested last year. I tried pulling the leg out on the extension, but it was not satisfactory, and during the last six months I have not done anything. I think I will leave it alone for some time, and then perform an oblique osteotomy of the upper end of the femur when the neck has become ossified.

Mr. H. A. T. FAIRBANK said that a few years ago he had published a similar case, in which the child died as a result of osteotomy; there was an infarct in one lung, the whole of which appeared solid at the post-mortem examination. There had been no more bleeding in that case than was usual in osteotomy, and he did not think he had had to use a single clip. In another case a child had died from a similar cause, as he (the speaker) was putting in the needle for the last suture. That was a case of resection for myositis ossificans. In the first of these cases there had been merely a small centre of ossification for the head. There had been no lack of cartilaginous continuity with the shaft; it was only that the neck had not ossified. In the patient now shown ossification in the neck would, he thought, gradually develop.

The other point of interest was the curve in the shaft, which was usually present in these cases, always showed dense bone, and was frequently mistaken for intra-uterine fracture. It was not intra-uterine fracture, however: one saw a similar curve in the tibia in cases of absent fibula. He did not think these were cases of fracture, nor could he see why fracture should occur. He agreed with the policy of waiting for a year or two and then performing an osteotomy to correct the coxa vara.

Lipoma in a Child aged 20 months.—CECIL P. G. WAKELEY, F.R.C.S.

Jean W. came under observation three weeks ago because her mother had noticed a swelling in the left loin which was thought to be growing larger.

On examination, a tumour the size of a chicken's egg can be seen, situated just above the crest of the left ilium. It is distinctly lobulated and can be moved on the deeper structures.

Anæmic Type of Hæmolytic Jaundice without Familial History.—F. PARKES WEBER, M.D., and M. SCHOLTZ, M.D.

The patient, Mrs. S. F., aged 34 years, was admitted to hospital on July 30th, 1930. A sallow, "puffy-looking" woman, with severe chronic anæmia, great weakness, mental apathy, ascites, splenomegaly, moderate variable fever, and very often obvious slight jaundice. The spleen reached down to umbilical level, the liver to three finger-breadths below costal margin. The galactose test (later on) for impairment of hepatic function gave a positive result. No enlargement of superficial lymphatic glands. No obvious subcutaneous œdema. Paracentesis abdominis (August 1st) yielded 7,500 c.c. ascitic fluid, of specific gravity 1008; positive Rivalta sign. Urine, on admission: specific gravity 1017: trace albumin; no sugar; no bilirubin; excess of uribilinogen; no tube-casts. Later, on August 4th, when there

[1] See *Proceedings*, 1929, xxiii (Clin. Sect.).

was definitely slight jaundice, the urine showed a trace of bilirubin. No ophthalmoscopic changes. Cardiac apex-beat, somewhat to left of nipple-line; apical systolic ("anæmic"), not permanent murmur. Brachial blood-pressure: 150/90 mm. Hg. Signs of fluid effusion in the right pleura; dry bronchitic sounds all over lungs. Later on (about middle of August) there was some temporary pleuritic friction at the back of the left lung. Blood-culture negative.

Blood-count (August 1st): Hæmoglobin 20 per cent.; erythrocytes 1,480,000; colour-index = 0·7; leucocytes 6,500 (eosinophils 1 per cent.; metamyelocytes 1 per cent; polymorphonuclear neutrophils 70 per cent.; lymphocytes 23 per cent.; monocytes 5 per cent.); one normoblast to 100 leucocytes; slight poikilocytosis; polychromatophilia; much anisocytosis (many megalocytes). The thrombocyte-count on August 8th was 132,240 per c.mm. of blood. Blood-serum: deep yellow colour; negative direct and strongly positive indirect Hijmans van den Bergh reaction. Excessive "fragility" of the washed erythrocytes: commencement of hæmolysis with a 0·72 per cent. sodium chloride solution. Negative Wassermann and Meinicke reactions. Fractional examination of the gastric contents (August 26th) showed achlorhydria, excepting after a subcutaneous injection of histamin (ergamine acid phosphate 0·001 gramme)[1]: then the free HCl reached 45 and the total acidity reached 63.

History.—The present extreme anæmia seems to have commenced about April, 1930. But when 13 years of age she was in the German Hospital from November 1909 to March, 1910, with severe anæmia, splenomegaly and jaundice (the notes were unfortunately destroyed). She married in 1928 and 16 months later had a still-born child: otherwise she has never been pregnant. She has been subject to "bilious attacks" without headache, and has sometimes been jaundiced, but never so much as in 1909. There is no evidence of any anæmia or jaundice amongst her relatives.

Progress in Hospital.—Under treatment by blood-transfusion (three times), iron, a liver extract for a long time, cardiac tonics (at first), and an acid pepsin mixture, her condition has varied a good deal. The pyrexia practically ceased about the middle of September. The spleen now (October 3rd) reaches down to the anterior superior iliac spine. The liver cannot be definitely palpated. No ascites or subcutaneous œdema. There is still great impairment of resonance at the base of the right lung. The cardiac apex-beat is still displaced somewhat to the left; no murmur. There is some chloasma uterinum, it should be noted, as there was on admission. (The patient has had amenorrhœa since June, 1930.) The sclerotics have a subicteric tinge. Blood-count on October 3rd (18 hours after a blood-transfusion of 300 c.c.): hæmoglobin 44 per cent.; erythrocytes 2,280,000; leucocytes 8,850 (basophils 1 per cent.; eosinophils 4 per cent.; metamyelocytes 5 per cent.; polymorphonuclear neutrophils 71 per cent.; lymphocytes 13 per cent.; monocytes 6 per cent.); two normoblasts to 100 leucocytes; polychromatophilia; no poikilocytosis; anisocytosis, with a good many megalocytes.

Paracentesis of the right pleura (October 4) yielded 445 c.c. deep yellow, clear serous fluid, of specific gravity 1025, giving a positive Rivalta reaction and a positive indirect but negative direct Hijmans van den Bergh reaction.

The case seems to be a very unusual one of hæmolytic jaundice (the extreme fragility of the erythrocytes never being present in any so-called Banti's disease), complicated by an infection (pleurisy, etc.), from which the patient now seems to be recovering.

Fistula behind Left Ear: ? Branchial.—ERIC A. CROOK, M.Ch.

E. W., girl, aged 5 years. Painless swelling behind left ear first noticed twelve months ago. The swelling burst externally and left a small opening, which has discharged clear fluid from time to time.

[1] Equivalent to one-third of a milligram of histamin.

Should anything be done in this case? The child seems to be none the worse for the fistula.

Discussion.—Mr. HAROLD EDWARDS said that the history seemed to be against the diagnosis of branchial fistula. The one or two branchial fistulæ he had seen were in the neck, in the anterior triangle, often with one or two hairs growing from the inner wall. His view was that this was a parotid fistula. Testing a little of the secretion would settle the diagnosis.

Dr. H. STANNUS said that the remnant of the first branchial cleft, persisting as what had been termed a helical fistula, occurred very commonly among natives of east central Africa.

Mr. CROOK (in reply) said that he had not been able to collect sufficient secretion to make a test.

Report on a Case of Carbolic Acid Poisoning.—JULIAN TAYLOR, M.S.

The case is reported in order to show the extreme rapidity with which carbolic acid may be absorbed through the skin, and that prompt treatment may be effective in reducing the intensity of the consequent poisoning.

On September 18th, 1930, a nurse had the misfortune to slip on a wet floor, upsetting in her fall a vessel containing a moderate quantity of "pure carbolic," i.e., acidum carbolicum liquefactum, B.P. The drug was spilt over a considerable area of her clothing, but as the accident occurred near an operating theatre where an operation was about to begin, the surgeon, Mr. R. M. Walker, was able immediately to remove the clothing and to apply large quantities of methylated spirit, the traditional antidote for carbolic acid burns. There was no question of associated head injury and at first the subject was able to assist in the removal of her clothing and to ask that spirit should be used, also oil for her eyes. In a very short time she was unable to sit up and her consciousness rapidly became clouded, and before three minutes from the time of the accident she was completely unconscious. Transferred to a ward, she was seen by me, in consultation with Dr. A. S. Wesson, less than ten minutes after the accident. She was then in deep coma, her four limbs and her face were continuously twitching, her pupils were semi-dilated and fixed, her colour was a greyish-blue and was visibly deepening, her respirations were laboured and bubbling, her mouth and nasal cavities were full of frothy mucus and no pulse could be felt at the cardiac apex or wrist. She had every appearance of being moribund. Her clothing had now been completely removed, she had been washed all over with large quantities of water and her conjunctivæ had been irrigated with normal saline. Her extremities rapidly cooled and her condition was clearly deteriorating. Thirty ounces of normal saline containing one drachm and a half of sodium bicarbonate were infused into a vein. During the infusion a definite effect was seen, inasmuch as from having been completely inert she began to toss about and to be difficult to restrain and at the same time to make inarticulate cries. The twitching ceased, the pulse began to be occasionally palpable at the wrist and by the time the venesection wound was being closed had definitely returned, though still small and very frequent. The insertion of stitches made her cry loudly, though she was still unconscious.

In about two hours' time she was completely conscious and reasonable. During the following twenty-four hours she vomited incessantly and continued to do so occasionally during the three days succeeding the accident. Her urine was at first dark green and contained albumin; it remained green for two days and albuminous for three. It was never diminished in quantity and microscopic examination failed to show the presence of any casts.

The burns, which were all superficial, were treated by the tannic acid method and, except for a small area on the right arm, remained almost everywhere dry. Nowhere was the whole thickness of the skin destroyed and only in the patch referred to were red papillæ visible.

The actual sites affected were the whole face and neck, the whole length of both upper limbs, the chest and upper abdomen, and small areas on the back and both lower limbs. The total area subsequently measured proved to be 3,340 square centimetres.

It is noteworthy that although for the immediate treatment of such an accident she could hardly have been more favourably placed (a surgeon with assistants and nurses being present at the time of the accident) and although the carbolic acid was washed off so promptly that nowhere the whole thickness of the skin was destroyed, yet absorption was so rapid that she was in deep coma before three minutes had elapsed. The changes in the skin were also of interest, the dead grey white of ischæmia in the earlier minutes changing to a dusky purple with the onset of general cyanosis. With the disappearance of the cyanosis the purple gave place to a dull red, suggesting vasomotor paralysis, and this in turn was followed by the brown discoloration of the dead cuticle. The shedding of the cuticle proceeded from the seventh to the fourteenth day, the underlying skin being then seen to have made a perfect recovery except in those patches where the deeper layers were affected.

The effect of intravenous saline was also striking, and is to be attributed either to dilution of the phenol content of the blood or to encouraging excretion by promoting a flow of urine, or just possibly to the presence of sodium bicarbonate. The change in the patient's condition while the infusion was taking place, from that of obvious decline to one of equally obvious improvement, was such that none of the observers had the slightest doubt that the improvement was the consequence of the treatment. It is partly for this reason that the accident is now brought to the notice of the Section. It is noteworthy also that she never had any suppression of urine such as may be a fatal consequence of carbolic poisoning. The traditional remedy of sodium sulphate was not used. It is stated by Sollmann [1] that the combination of sulphates with phenol to form the innocuous sulpho-carbolate is so slow a reaction as to be useless where a rapid effect is wanted, as must usually be the case.

Popliteal Aneurysm.—HAROLD EDWARDS, M.S.

Patient, male, aged 34, cobbler. Nine days before admission into hospital had pain in left leg and difficulty in walking. Two days later noticed slight swelling behind knee. This increased rapidly, and became very painful.

Condition on Admission into King's College Hospital, September 19, 1930.—Large pulsating swelling occupying right popliteal space, pulsations being synchronous with heart-beat. Overlying skin hot, tense, and slightly reddened; digital compression over femoral artery reduced size of swelling and caused pulsation to cease. Diameter of limb at site of aneurysm before compression was $15\frac{1}{2}$ inches; after compression $14\frac{1}{2}$ inches. Loud bruit on auscultation. Dorsalis pedis artery on same side could be felt only with difficulty. Pulse easily obliterated. Heart sounds normal.

September 27, 1930.—Femoral artery ligated in Hunter's canal.

The patient has no other signs of cardiovascular disease. The blood-pressure is 118 systolic and 52 diastolic.

At his work he sometimes sits in a low chair and at other times stands. He steadies his last by means of a stirrup with a rope attached, and this keeps his left foot three inches from the ground. The clinical evidence of syphilis is at variance with the test; there is iritis in the left eye but the blood and cerebro-spinal fluid are Wassermann-negative.

Discussion.—Dr. M. CASSIDY said that during the last summer he had seen a man, aged 50, who had a popliteal aneurysm on the right side. Nothing else was found wrong—

[1] Sollmann, "Manual of Pharmacology," W. B. Saunders, 1926, 633.

except that the left popliteal artery was somewhat enlarged. The right femoral artery was successfully tied, but within a fortnight of that procedure a definite popliteal aneurysm developed on the left side. This grew rapidly, and it was decided to tie the left femoral artery. The patient was anæsthetized in the theatre, and when being examined under the anæsthetic, was found to have a common iliac aneurysm, and it was therefore decided not to proceed further. Subsequently an abdominal aneurysm developed which ruptured and from which the patient died, within two months of the appearance of the first popliteal aneurysm. The Wassermann reaction was negative.

Mr. C. P. G. WAKELEY said he thought that the comparative rarity of aneurysms at the present time was due to syphilis being more promptly and thoroughly treated than years ago.

Tuberculous Disease of the Sternum.—CECIL P. G. WAKELEY, F.R.C.S.

E. L., female, aged 33, first noticed a swelling over front of chest six months ago. This has been gradually growing larger. It was painful when the patient coughed. In September, 1930, it broke down and discharged some blood-stained fluid.

At the present time there is a large ulcerated surface with definite undermined edges over the manubrium sterni and angle of Louis.

Examination of chest shows tuberculous infiltration of right apex and upper zone.

When the patient came in, the ulcer was fluctuating and had broken down. During the summer she had positive sputum. The Wassermann reaction was negative. These cases are not common, and there is a difficulty in treatment. I have seen one or two which have been operated upon by my colleagues. An extensive ulceration has been left, and the patient has had from five to ten sinuses afterwards. There is a tendency for this condition to penetrate more deeply into the sternum and get into the mediastinum, and I wonder whether there is any form of treatment except surgery for such cases, as the skiagrams reveal nothing except some thickening in the sternum.

Discussion.—Mr. C. E. SHATTOCK said he would advise treatment by diathermy.

Mr. JULIAN TAYLOR asked upon what the diagnosis of tuberculosis of the sternum was based. Mostly, he thought, tuberculosis of the chest wall meant mediastinal foci of disease coming through the intercostal spaces. On exploring these cases one found there was no diseased bone. Sanatorium treatment was, he thought, indicated.

Mr. WAKELEY (in reply) said the diagnosis must be made by taking some material from the edge of the ulcer and examining it microscopically. He did not think there was a definite hole in the sternum, and the lateral skiagram showed the sternum to be thick, with no tracts at all. He agreed with Mr. Taylor that the disease had probably come from the anterior mediastinum and through more than one or two foci.

Aneurysmal Angioma of Brain.—CECIL P. G. WAKELEY, F.R.C.S.

A. W., female, aged 52, came under observation two weeks ago, complaining of severe pains in the head. Headaches began eight years previously and have gradually increased in intensity. During the last year patient has noticed a definite whistling noise in the back of her head. Pain is worse when she is lying quietly in bed. Three years ago she was compelled to use spectacles for reading and near work; now has to use spectacles for distant vision also, and reading is impossible for more than three minutes, as it aggravates pain at back of head.

About six months ago a small swelling appeared in the region of the external occipital protuberance; this has gradually increased and is now the size of a chicken's egg. It is soft and pulsating and a marked bruit can be heard all over back of skull.

Patient is deaf in the left ear, probably owing to chronic otitis media, as a polypus was removed from that ear when she was a child, and following the operation there was a persistent aural discharge for thirty years, ceasing after that time. No history of trauma to skull.

Patient looks well. Blood-pressure 130/90. Abdominal reflexes present; knee- and ankle-jerks normal on both sides. Pupils equal: react to light and

accommodation. Eye movements free. Good convergence. R. eye, 2° latent convergence. L. eye, 2° latent divergence. Vision, right eye = $\frac{6}{9}$ with + 0·50 D. sph. = $\frac{6}{6}$. L. eye = $\frac{6}{12}$ with + 0·75 D. sph. = $\frac{6}{6}$.

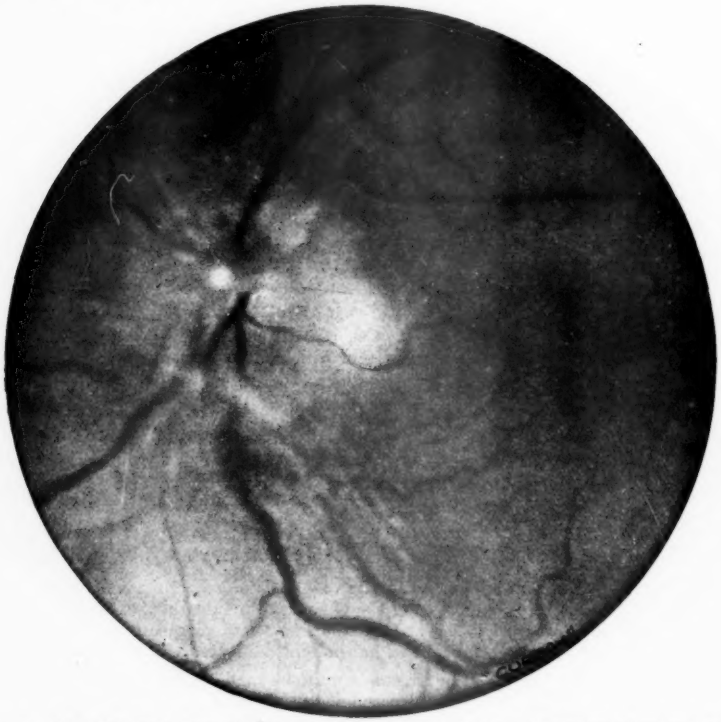

FIG. 1.—Mr. Wakeley's Case of Aneurysmal Angioma of Brain. Dilatation of retinal veins.

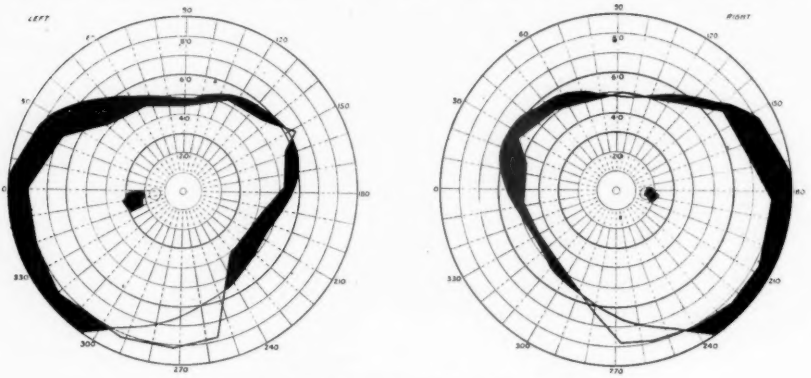

FIG. 2.—Aneurysmal Angioma of Brain. Visual fields.

Discs on both sides choked; considerable blurring of edges and a certain amount of exudate. Retinal veins dilated (fig. 1).

Fields of vision somewhat limited; blind spot deflected outwards (fig. 2).

Skiagrams of skull, taken by Dr. Graham Hodgson, show dilated meningeal and diploëtic vessels. Antero-posterior skiagram reveals large defect, size of half-a-crown, in occipital bone just above external occipital protuberance (fig. 3).

FIG. 3.—Aneurysmal Angioma of Brain. Antero-posterior view showing defect above the external occipital protuberance.

Dr. Macdonald Critchley has ascertained for me that the murmur is not louder when the patient is reading.

Discussion.—Mr. C. E. SHATTOCK said he regarded the tumour as an angiosarcoma. The pulsation was not so striking as in ordinary aneurysm; he could not feel any tortuous vessels, and the appearance in the skiagram suggested malignancy rather than aneurysm eroding the skull.

Dr. MACDONALD CRITCHLEY said that the case recalled one published by Dr. Fulton (*Brain* 1928, li, 310) in which there was an arterial angioma of the occipital lobe. There had been a well-marked bruit audible through the stethoscope, varying in intensity according to the patient's activity. When the eyes were closed the bruit was considerably hushed, but it became louder as soon as the patient began to read, suggesting that visual effort was associated with an increased blood-supply to the visual cortex. He (Dr. Critchley) had tested this present patient in the same way but was unable to convince himself of any alteration in the bruit. He thought the tumour was more like an angioma than a sarcoma, on account of a shadow in the skiagram due to a large vessel passing into the area of erosion.

Dr. FERGUS FERGUSON said that despite the fairly extensive "decompression" defect made by the tumour in the skull, and the vascular connections of the neoplasm, a high grade of papillœdema had developed.

Dr. PARKES WEBER suggested that the tumour might be hæmangiosarcomatous.

Mr. WAKELEY (in reply) said that such tumours had produced thinning. The patient's doctor had thought that the swelling was an abscess and, as he had been alarmed by the hæmorrhage when he dealt with it, he had sent her to hospital. If the angioma was on the surface of the brain, he (Mr. Wakeley) did not think that tortuous vessels would be apparent.

(The report of other cases shown at this meeting will be published in the next issue of the *Proceedings* of the Section.)

Section of Urology.

President—Mr. S. G. MacDonald, F.R.C.S.

[*October* 23, 1930.]

PRESIDENT'S ADDRESS.

The Results of Partial Resection of the Bladder for Carcinoma.

By S. G. MacDonald, F.R.C.S.

When examining a growth of the bladder with the cystoscope, the first question that arises is whether the growth is benign or malignant. A satisfactory clinical (or cystoscopic) classification of these growths is difficult. I divide them in my own mind into three groups: (1) Growths which are probably benign. (2) Growths which are certainly malignant. (3) Growths of doubtful nature.

(1) *Growths probably benign.*—These are the single pedunculated papillomata occurring in young subjects, e.g., under 40 years of age. This age is purely arbitrary, as it is impossible to say with certainty that any given papilloma is benign, even under this age: whereas over this age every papilloma must be regarded with suspicion. Probably 50% of all papillomata of the bladder are primarily (or "inherently") malignant, and the rest, if untreated, acquire a secondary malignancy after varying periods.

(2) *Growths certainly malignant.*—These are: (*a*) Bald growths. (*b*) Squamous-celled carcinomata. (*c*) Infiltrating and nodular growths.

(*a*) The bald growths—so called from their cystoscopic appearance—are sessile growths, often covered with phosphates; microscopically they are papillary carcinomata in which the spaces between the papillæ have become obliterated; or, maybe, adjacent papillæ have fused, so that a bald solid growth results; later these form one type of "infiltrating" growth.

(*b*) A squamous-celled carcinoma appears, cystoscopically, as a typical epitheliomatous ulcer, with a thickened everted edge and necrotic base.

(*c*) The infiltrating or nodular growths occupy a larger portion of the bladder wall than do the first two kinds. They are hard on palpation, their surface is irregular, and there may be large masses projecting intravesically; ulceration of areas of necrosis may be present.

Histologically these infiltrating growths are difficult to classify, as various types of cell are found, from the normal transitional bladder epithelium, to ordinary spheroidal-celled carcinoma. The latter may be alveolated and highly cellular, or of the scirrhous type.

Adenocarcinoma is a rare type arising in mucous glands in the region of the trigone and internal meatus (suburethral glands of Albarran).

(3) *Growths of doubtful nature.*—This category comprises most papillomata occurring after the age of 40, and their correct treatment is, to my mind, one of the most difficult questions in urology. Their base is broad and sessile rather than pedunculated, the villi are short and stunted—the shorter the villi, the more likely is the growth to be malignant. Other points favouring malignancy are the presence of ulceration or necrosis, or incrustation of the growth with urinary salts, the presence of puckering or œdematous bullæ round the growth, or the presence of outlying nodules beyond the main growth—all these denoting infiltration of the underlying tissues.

Multiplicity of growths is a doubtful diagnostic point; if two or three papillomata are present they are probably benign; of course one papilloma may have undergone malignant change, so that one finds benign and malignant growth in the same bladder, and I have several times experienced a benign recurrence following excision of a malignant papilloma, but when a stage of general papillomatosis is reached they are certainly malignant. Implantation growths of bladder secondary to renal papillomata are always malignant.

The histological diagnosis of some of these doubtful growths appears to be just as difficult as their clinical diagnosis. Certainly I have had several returned as benign which subsequently, and rapidly, proved malignant. This raises a suspicion that some of those returned as malignant may have been benign. Infiltration of the base of a papilloma proves its malignancy, but the converse is not necessarily true, i.e., absence of infiltration does not mean that it is necessarily benign. Here for example is a report recently received:—

"This shows a stumpy papillary growth; though not apparently inclined to infiltrate, it is composed of *cells of malignant type.* Histologically it must be considered malignant. I emphasize "cells of malignant type," as their recognition must be the ultimate test.

Situation and extension.—The lymphatics of the bladder arise in an intramuscular network and a superficial network on the outer surface. Trunks from these networks drain into the external and internal iliac glands; those from the anterior surface and the upper part of the posterior drain into the external iliac chain (lying between the crural ring and the bifurcation of the common iliacs). Those from the middle portion of the posterior surface run directly backwards to glands on the promontory of the sacrum at the bifurcation of the aorta; while those from the lower part of the posterior surface and the internal meatus run—with those from the upper surface of the prostate—along the upper aspect of the vesicles and along the vasa deferentia to the internal iliac chain: not infrequently there are interrupting nodes along this chain, and these are the first glands to be involved in carcinoma of the bladder base; in the latter case they may be palpable on rectal examination.

These growths originate chiefly at the base of the bladder, in close relationship with one or other ureteric orifice: extension therefore is found chiefly at the base; the prostate, prostatic urethra, vesicles, uterus, pelvic bones and lumbar vertebræ may be invaded—rarely the vagina and rectum. As spread is by way of the intermuscular lymphatics, the invasion of the bladder wall may be much greater than the actual extent on the mucous surface revealed by cystoscopy. Regional glandular involvement is late (and ? uncommon); certainly in many inoper-

able cases the glands are found uninvolved, and death often supervenes (from uræmia, hæmorrhage, or sepsis) before any general metastasis has occurred. The commonest sites for metastases (apart from the pelvic bones), when they do occur, are the pleuræ, lungs, liver and spleen.

Symptoms.—In about 80% of cases the first symptom is hæmaturia; in the rest, hæmaturia supervenes upon a chronic cystitis. Usually hæmaturia is an early symptom, rarely it occurs late. I shall refer to this question again.

Scope of operation.—Operation aims at removing the growth with a sufficiently wide margin of the whole thickness of the bladder-wall—one inch margin at least is aimed at—and avoiding implantation at the time of operation. Growths close to the internal meatus, where a sufficient margin cannot be obtained, are inoperable. When the growth involves a ureteric orifice, or is so close to it that a sufficient margin cannot be obtained otherwise, the ureteric orifice and the lower end of the ureter are removed also, and the ureter is transplanted elsewhere into the bladder. No elaborate dissection of the ureter from outside is necessary; the portion of the bladder to be resected is isolated gradually, beginning from below, and the ureter is recognized readily during the course of the dissection. In many cases it is considerably enlarged. The added risks of ureteric transplantation will be referred to again.

Implantations are best avoided by cauterizing the surface of the growth before excising it, and by doing the actual excision with the endothermy knife, which has the additional advantage of speed by reducing hæmorrhage.

When the growth involves the peritoneal aspect of the bladder the peritoneal cavity must be opened, and a corresponding portion of peritoneum removed; with peritoneal invasion the omentum is usually found adherent to the growth, and in these cases dissemination is rapid.

It has been stated already that the muscular involvement of the bladder may be much greater than its intravesical extent as shown by the cystoscope. Doubtful cases should be given the benefit of the doubt by suprapubic exploration.

Successful resection should be followed by a full course of deep X-ray therapy as soon as the patient is convalescent.

Results.—Of growths "certainly malignant" I have notes of 120 cases: 35 operable, 85 inoperable. Of "growths of doubtful nature" there are 55; 20 (36·36%) proved on subsequent microscopy to be malignant and 35 benign (63·63%). This gives a total of 140 cases of carcinoma of the bladder to date; 55 (39·28%) operable and 85 (60·71%) inoperable.

For purposes of statistics I am taking the cases over a period roughly of eleven years, ending 1927, all of which have gone three years since operation. During this period 46 operable cases were seen; two patients refused operation, leaving 44 actually operated upon. Their ages varied from 31 to 74, average age 57·13. In the cases of "doubtful growths" which proved to be malignant, the patients were younger than in those which proved benign (48-79, average 60). There were 34 males (77%) and 10 females (22%).

The immediate mortality comprised six cases (13·63%); this includes all that died in nursing home or hospital: one on the table from cardiac failure; one from pulmonary embolus (third week); one from cardiac failure (twelfth day); one from ileus; one from pyelonephritis (thirty-seventh day); one several months later with growth fungating through the wound.

Within the next three years I know of fifteen deaths—all with recurrent growth except two (one from pyelonephritis four months later, the other, suddenly, from heart disease twelve months later); nine cases I have been unable to trace. This leaves fourteen alive and well at the end of three years—or 31·81% cures, if the three-year standard is adopted.

I fear, however, that even this is an optimistic figure; the three-year standard is much too short, as two of these fourteen subsequently developed a local recurrence, one seven years and another nine years after operation. There is also the possibility of error in the histological diagnosis of some of the "doubtful growths." Of the forty-four operated upon, the ureteric orifice and the lower end of the ureter were resected in twenty, of whom three died from pyelonephritis (two, three and four months respectively after operation, and whose death was directly attributable to the resection of the ureter; all these had bladder infections before operation). Resection and transplantation of the ureter involve two risks, firstly that of ascending infection, and secondly that of constriction and hydronephrosis. My statistics show that the former risk adds considerably to the gravity of the operation when the bladder is already infected but not when it is aseptic. Thus in the series of thirty-five "growths of doubtful nature" which microscopy subsequently proved benign, and in which partial resection of the bladder was performed, the ureteric orifice and lower end of the ureter had been resected in ten, of whom all survived. I think the second risk, that of contraction and hydronephrosis, is not a serious one. I had the oportunity of making a post-mortem examination on one patient nine years after operation. In this case the ureter and kidney were a little dilated, but not more than might have been caused by the original growth before resection. Certainly in many cases the ureter is found dilated at the time of resection, and one of my patients had a large hydronephrosis caused by the bladder growth.

One notable point in this series is the large number of cases which were inoperable when first seen, viz., 85 out of 140 or 60·71%. Had I included the cases seen in my out-patient department the proportion of inoperable cases would be higher still.

The average duration of symptoms in the operable cases (excluding those supervening upon chronic cystitis or previous papillomata) was, roughly, seven months; in the inoperable cases it was fourteen months. These facts speak for themselves, but may be a little misleading, as in several of the inoperable cases there had been no hæmaturia until three or four weeks before cystoscopy. Every case of chronic cystitis and every case of hæmaturia should be subjected to cystoscopy.

In judging the prognosis of each individual case after operation, the pathologist is most helpful; the main points being the type of cell present and whether the margin is wide of the area of permeation. Better results will be obtained in the future by securing the cases earlier and by a wiser selection. I have operated upon all in which I judged excision possible. Some, I fear, had an insufficient margin and were not worth while.

I invite the views of Members on the treatment of "growths of doubtful nature." Should they be treated by diathermy, through the cystoscope, and watched—only being resected when their malignancy seems assured—in which case much valuable time is lost? Or should they all be resected at once, in which event many benign ones will be subjected to unnecessary operation?

The high proportion of malignant growths in this group (36·36%) inclines one to advise the latter course.

Discussion.—Mr. FRANK JEANS said that he felt depressed about the results in malignant growths of the bladder. He quite saw the difficulty concerning the President's "doubtful group." He had been struck by the fact that sometimes a growth on the roof of the bladder seemed to be operable, and a large amount of bladder was removable from that site, and yet there was recurrence.

He agreed that the part of the bladder which had a peritoneal covering and had omentum attached to it was the worst possible site for a growth. Taking a parallel case, it was useless to resect a colon which had become adherent, by carcinoma, to the stomach. As soon as one carcinomatous cell got into the peritoneum, it was in the current of the largest lymph system of the body, and there might already be secondary deposits in the spine, and other places.

To diagnose between a malignant and an innocent growth through the cystoscope was, he agreed, a matter of great difficulty. He, personally, had an elementary guide: the greater the amount of deposit of salts and phosphatic accretions on the growth, the more likely was it to be malignant, and a clinical history of hæmaturia was important. The condition in a patient who had what Moynihan called the " steeple " chart of gall-bladder, was more likely to be innocent than when the blood-chart came up slowly and went down slowly; in the latter case it was more likely to be malignant.

In dealing with the kind of growths under discussion it was necessary to be ruthless in resection. There was, he considered, a danger of implanting the ureter into the bladder.

He did not know whether the President had been troubled with fistulæ following these operations. His own experience of fistulæ from the ureter tended to make him quite conservative. On several occasions the fistula had closed itself after any period from three weeks to six months; in one case it was eight months.

Mr. JOHN EVERIDGE said that with regard to the danger of the apparently simple growths which were situated near the top of the bladder, and which the surgeon thought would be especially suitable for operation: recently, at King's College Hospital such a case was seen in a female. The growth was apparently suitable for operation; it looked like a bun stuck on the top of the bladder with the cystoscope. Owing to its solid nature it was diagnosed as carcinoma. It was operated upon and there was found to be a great mass which involved the muscle and the peritoneum. It also extended back and was adherent to the uterus. It proved, of course, entirely inoperable.

He had not yet come across a case of fistula following ureteric resection and transplantation. He had operated upon many of these cases, and the results had been good. An important matter in the technique of the operation in which the ureter had been incised or resected was to carry out prolonged drainage in the neighbourhood of the ureter. In cases of resection of the lower end of the ureter, the drainage tube should be left in the cellular tissue round the lower end of the ureter for at least ten days; there was then likely to be better healing of the ureter, and suppuration was less likely to occur.

He had brought for inspection a specimen from a case in which, in 1922, he had resected the right side of the bladder and implanted the ureter. The disease was nodular carcinoma. The case had done very well. At the end of the operation the bladder was very small, as such bladders always were. Healing was rapid, and the patient was passing water well three weeks afterwards. Two months after the operation the urine could be retained for four hours. This patient had a great friend who developed cancer five months after the operation described, and this so worried the patient that he shot himself. The suicide took place near the hospital and so there was an opportunity of carrying out a post-mortem examination, and the bladder was rescued. It was healthy, and the ureter opening was good. The ureter was dilated and this dilatation had probably existed before the operation, because the growth was situated right over the opening, and had caused obstruction.

Mr. RALPH THOMPSON said that he had been sorry to hear the President's remarks about implantations occurring at the time of operation; he thought these referred to the surgeon who did scrapings of bladder growths, not to the expert urological surgeon who performed excisions.

With regard to secondary deposits: In cases of carcinoma of the bladder these were uncommon. In the course of twenty years, during which he had seen about ten thousand cases of all kinds at hospital, he had hardly seen one in which there were secondary deposits. The fact was that many patients with bladder growths died from ascending nephritis, and the sooner this was generally recognized he thought the better.

Concerning the President's case, in which death occurred while the patient was under the anæsthetic, before the operation was well started, he (Mr. Thompson) was willing to defer to the President in regard to the time, but he would say that deaths under anæsthesia when the bladder was opened, were not uncommon, and, considering the statistics, one could not greatly blame oneself because the patient died before the growth was reached.

He considered that the President was right in advocating open operation as the treatment for carcinoma and papilloma. He (the speaker) would not say that diathermy was not useful, but it would be found that 75% of the people who used diathermy were not expert

bladder operators. Diathermy might be a useful method of treatment, but much patience was needed on the part of the patient to make it a success. As a general rule he did not think diathermy was as good in its results as was open operation.

Referring to the situation of the growth in the bladder, it was very interesting that, as a general rule, growths of the bladder, of innocent nature, usually occurred outside and above one uteric orifice. Those with experience of cystoscopy knew that the flow of urine was directed upwards and outwards as it passed from the ureter, and that could only be seen with the cystoscope. He remembered making an admirable demonstration in the presence of Professor Laidlaw, proving that such was the case. Two hours after the death of the patient he had injected the bladder through the urethra with white plaster. Before the plaster had set he had cut down on the left ureter and injected it with blue plaster. When sections were cut of the plaster cast of the bladder after it had set, it was remarkable to see the way in which the blue plaster curved over and came to the outside of and above the left ureter. These observations indicated that a growth occurred where the urine coming from the ureter impinged against the bladder-wall. When there was a growth of the bladder his own practice had always been first to excise it, and then, if there was a recurrence to employ diathermy. The results of this policy had been good. A few days ago he had met a man upon whom he had operated seven years before for a growth in the bladder. The growth had been situated above and outside the left ureteric orifice, and had been diagnosed by Dr. G. W. Nicholson as malignant. There was no evidence of any recurrence, but he thought the evidence Dr. Nicholson gave as to malignancy—that the growth infiltrated—was not quite satisfactory. What did it infiltrate? He (Mr. Thompson) had only cut through the pedicle. Some of these pathological reports with regard to infiltration should be accepted with caution.

He would insist that the surgeon was justified in excising these growths and telling the patients they must be prepared to go turough with the operation, rather than in attempting treatment by diathermy and other methods to which inefficient operators resorted in many cases.

Mr. JOCELYN SWAN said that, to all engaged in urological work, the group of cases which the President designated as "doubtful" were very important, because it was certain that whereas one could get, on the one hand, the obviously simple growth, and, on the other hand, the obviously malignant one, the difficulty was to diagnose accurately the nature of those in the "doubtful" group. A point on which he had placed a good deal of reliance was the fact that small areas of sloughing or necrosis on the surface of these growths were very important signs of malignancy. Another diagnostic point upon which he relied in these cases was obtained by the use of diathermy. A point first emphasized by Mr. Swift Joly some years ago was that if, when one began a treatment of what was apparently a simple growth, on putting the active diathermy electrode into the growth for some seconds and on withdrawing it, the growth was found not to draw away from the bladder wall, infiltration was probably occurring in the base of the growth. In such an event, the sooner the surgeon abandoned the diathermy treatment and proceeded to open operation and resection the better. In some of these small villous-covered growths such small points helped considerably.

In every case in which there was a doubt whether the evidence favoured malignancy or innocency, but in which malignancy was the more likely, the growth should be resected; there should be no attempt to treat it by cystoscopic diathermy.

One taught that in looking at villous-covered growths through the cystoscope one must carefully observe the condition of the mucous membrane around the pedicle, but the more we saw of these growths the more we appreciated the difficulty of seeing the area immediately surrounding the pedicle.

He was not a great believer in diathermy, except for small, unmistakably innocent growths. It was necessary to have in mind a standard of size, and his own limit was one of the size of an ordinary cherry. A growth larger than this was better treated by resection than by diathermy. He used the diathermy for small tumours and for recurring growths which he felt sure were innocent papillomata. In many cases diathermy used through a suprapubic vesical opening was preferable to that used by means of a cystocope.

With regard to the histology of these growths, he did not think great reliance should be placed on pathological reports, as even eminent pathologists had great difficulty in telling whether they were really malignant or not. Many growths which, clinically, he (the

speaker) would not hesitate to call malignant, from the appearance found at the operation, were reported by the pathologist to be innocent; conversely, growths which had all the clinical aspects of innocency were occasionally reported to be malignant. This made one's statistics very difficult. He was inclined to place more weight on the aspect and appearance presented at the operation than on the pathologist's report as a guide to the nature of the growth. He looked upon every villous-covered growth in the bladder, even those which at first had the appearance of being benign, as an extremely serious condition; he regarded them as pre-cancerous, if not already malignant. He had now operated upon a number of cases in which one, two or even three recurrences were innocent, but a further one was undoubtedly malignant.

In the treatment of these cases, too, there was a point of interest concerning metastases. The infiltrating epithelioma or the adenocarcinoma of the base of the bladder showed a fairly rapid spread to the glands, going thence by the pelvic lymphatics, which might be felt per rectum as a thickening passing upwards and outwards above the prostate, and before long the glands were found to be involved. In the villous-covered tumours, however, metastases in the glands were very late. Looking at the matter on general lines: In dealing with malignant disease in any part of the body one could say that in the case of a growth which was expending its energy in forming a cauliflower type, metastases occurred only very slowly, but that in cases of epitheliomatous and infiltrating forms, metastases occurred early.

He agreed with the President about the wide removal of the base of these growths; removal must be wide and must include a good, clear area of healthy mucous membrane and vesical wall round the base of the growth. He did not hesitate to transplant the ureter; he had done so many times, and he had not yet seen the procedure followed by fistula, nor had he had to operate subsequently for hydronephrosis. He agreed with the President that the operation increased the risk of ascending sepsis of the kidney if the bladder was in a septic condition. He did not hesitate to transplant the ureter if it came within the field of the resection. A point which had been a great help to him was, that when he had the bladder open he passed a catheter into the ureter before attempting resection. That was useful in two ways: occasionally it helped to identify the distal end of the ureter, and towards the end of the operation it was one of the last things to bring up and divide.

He also agreed with Mr. Everidge's recommendation to leave a space in the cellular tissue in the bladder alongside the ureter, which had been transplanted, and to drain it. That avoided the possibility of stenosis of the opening of the ureter, or of cicatrization above, which might lead subsequently to obstruction.

Mr. E. W. RICHES said that he would quote two cases illustrating the value of palliative treatment when more heroic measures were not advisable, owing either to the local condition of the growth or to the general condition of the patient.

The first case was that of a woman, aged 66, who came to Middlesex Hospital in June, 1927, with a two years' history of hæmaturia. She was operated upon by his (the speaker's) chief, who found a large papilliferous type of carcinoma; it arose above and outside the right ureter, and was spreading across the base of the bladder. The growth was inoperable locally, and he did not think that the patient's general condition was such as to bear a large resection. The growth was removed superficially, purely as a palliative measure, with the idea that it might relieve the hæmaturia, though it was probable that there would be a recurrence. The growth was examined microscopically and was reported to be malignant, and in a few months' time there was a nodular recurrence, which was further over to the left of the bladder. He treated it, per urethram, by diathermy. That was over three years ago, and the patient had been attending hospital regularly, and had had diathermy treatment through the urethra five times during the three years. Since her operation she had put on three stone in weight, had had no further hæmaturia, and was now able to hold her urine, passing it only once or twice in the night, and holding it for three hours in the day. In this case the less heroic measures had been entirely justified; if an attempt had been made to resect that patient's bladder she would probably not now be alive.

The other case was that of a woman, aged 75, who had come to him a year ago with a typical epitheliomatous ulcer of the size of a five-shilling piece above and outside the right ureter. After a cystoscopic examination he had opened the bladder and found that the whole of the wall was adherent and that the growth was infiltrating. He took out a piece of the growth for the purpose of examination—which confirmed malignancy—and inserted radium, using a

smaller dose than usual, namely ten 0·5-mgm. tubes, with 0·5 mm. of platinum screenage, leaving those tubes in five days; they were arranged radially from the outskirts of the growth. The wound was dry on the fourteenth day; in most cases when radium was put into the prostate or bladder from the mucous surface, healing was considerably delayed. He again examined the patient cystoscopically a month later, and there was then a large slough covering the whole area of the growth. There was also a piece on the edge which looked suspicious, and was therefore diathermized. He made a further cystoscopic examination (five months after operation) and the slough was still present. Diathermy was again applied around the growth. Last week—she then being aged 76—her doctor reported that she was up and about and well, on only two occasions having had slight hæmaturia.

Those two cases had been treated on palliative lines. It was not expected that they would do well, but they served to show that it was always worth while to try to do something for the patients in these cases, even though that something was not a properly-planned operation for malignant disease.

Mr. ZACHARY COPE said that a kind of growth which had not been touched on was that which infiltrated in the region of the internal urethral orifice. Did urological surgeons consider that, in a feeble patient, a considerable excision of such a growth in this sensitive part was the best course to follow, remembering that radical treatment showed a considerable mortality?

He would instance two recent cases. One was that of a man aged 78, who came to him because of retention of urine caused by a growth blocking the internal urethral orifice. He had had hæmaturia and complete retention. The prostate was not enlarged, but there was an infiltrating growth at the urethral orifice. The speaker first diathermized the growth by open operation and then inserted radium. The bladder healed up well, and he had seen the patient from time to time since, the last occasion being ten days ago. He had remained comfortable ever since the treatment and had put on over two stone in weight. Probably he would not have been in such good condition if the whole neck of the bladder had been excised.

The other patient was a woman whom he saw a year ago because of severe hæmaturia. On cystoscoping he could not see anything, but when he opened the bladder he found it to be full of growth. He removed this material, which weighed 12 oz. It was a growth which he would have had considerable hesitation in removing by the knife, but he cut it away piecemeal with the diathermy knife. It had a base the size of a five-shilling piece, near the internal urethral orifice. He carefully diathermized this case and had seen the patient from time to time afterwards. She had been comfortable during the year since operation.

He would plead for the intelligent use of diathermy; skill was required in order to employ it correctly.

Mr. F. MCG. LOUGHNANE said that when surgeons used diathermy it was not because they were afraid to operate; they did so from choice. If one was able to remove these doubtful growths of the bladder as completely as in cases of cancer of the breast or the uterus, taking away also the whole glandular area, one would operate, but in the bladder region this could not be done. At best, the procedure in these cases was merely palliative. If they were tackled first with diathermy, the growth was destroyed and the mucous membrane healed up. It was then easier to know whether one was dealing with a simple or with a malignant growth, and if it proved to be malignant it was easier to carry out extirpation. Many of these growths turned out to be simple, and it was better to give the patient the benefit of the doubt by carrying out a diathermy operation, which only needed to be performed twice according to the degree of skill of the operator. Then one could deal with whatever condition remained.

Mr. RALPH THOMPSON, in reply to criticisms of his remarks on the use of diathermy, said that the Members who had taken up his challenge belonged to the 25% of skilled operators that he had indicated.

Mr. BERNARD WARD said that he supported Mr. Zachary Cope's opinion in favour of occasionally using open diathermy. He was opposed to meddlesome cystoscopic diathermy carried out on growths requiring repeated applications which were apt to tire the patient out. In all cases of multiple or large growths he had for years made a point of treating them

by diathermy through the open bladder and his results had been comparatively good. It had been surprising to see how some huge growths—sometimes the size of a hen's egg, sometimes multiple growths almost filling the bladder—reacted to diathermy, without resection being performed. He had had many such cases in which he had cut off the growth with the diathermy knife and charred the base, leaving a deep slough to come away, and there had been no recurrences. In some cases there had been recurrences in other parts of the bladder, which had subsequently yielded to diathermy through the cystoscope. Wherever possible, he followed up his cases for some years—every three months during the first two years; if he saw a sign of recurrence he touched the growth with the diathermy point. During open operation one must take precautions against dissemination, making sure that no pieces were broken off and entangled in the wound or in the fat beneath the peritoneum. In one of the first cases he had treated in this way the growth was a simple papilloma, but carcinoma had developed in the upper end of the wound, outside the bladder, from a piece of the growth which had become enmeshed in the extra-peritoneal fat. The patient had died from secondary deposits, not from the bladder, but from the secondary carcinoma. He always took care to char the surface of the growth thoroughly before it was dealt with, and then he dissected the base, or left it to slough away. In a number of cases he left the base without dissection, and though they were reported as malignant papilloma there had been no recurrence.

He had noticed an increasing laxity in the definition of malignant growths. A definition which, he considered, always held good, was as follows: "A malignant growth is one which transgresses the basement membranes." From an examination of the surface of the growth, no pathologist could say whether it was or was not malignant; that the cells showed or did not show mitosis, that the layers were multiple or single, or that the fimbriæ coalesced or remained discrete, was not sufficient evidence. This uncertainty was one reason why it was difficult to prepare statistics. The infiltrating growth showed a very high percentage of recurrence whatever the treatment.

The PRESIDENT (in reply) said that Mr. Jeans had raised the question of ureteric fistula after ureteric implantation. He, personally, had been fortunate in never having encountered such a case.

Mr. Everidge had stressed the importance of prolonged drainage. He (the President) always drained outside the bladder after transplantation, but not for a longer time than three or four days. The bladder was a very accommodating organ when it was a matter of resection: one could cut it about freely, and yet it seemed to be all right in the end.

Mr. Ralph Thompson had said that the cause of death in these cases was sepsis and ascending pyelonephritis, and with that opinion Members would agree. In his paper he (the speaker) had said that hæmorrhage, sepsis and uræmia were the main causes of death. Most patients died from one of those causes before general metastases had had time to develop.

As to deaths under anæsthesia, he did not think that the danger was at the time of the opening of the bladder, it was when the patient was placed in the Trendelenburg position; in that regard it was necessary to be very careful in some of these cases. The patient whom he had mentioned had been overhauled by a physician the day before the operation. He was aged 60, and had a fairly high blood-pressure and normal heart sounds. Yet he died suddenly when placed in the Trendelenburg position. When his heart was examined it was found to be soft and fatty, and the finger could be pushed through its walls. He did not know whether there were means of recognizing such heart conditions beforehand.

Mr. Ralph Thompson had further said that patients on whom diathermy was practised had to be *very* "patient." In any case in which he (the speaker) had treated a growth by diathermy the patient had been under a general anæsthetic, and, so far as practicable, he had removed the growth at one sitting. From experience one was able to judge pretty well whether one had completely destroyed the growth, and an examination could be made three weeks afterwards to make sure. If the growth were dealt with by diathermy piecemeal, it might beat one in the end. In all attempts to treat these cases by diathermy the patient should be under a general anæsthetic.

Mr. Jocelyn Swan appeared to agree with him (the President) on the main points, especially as to the inherent malignancy of papillomata, and was in favour of operation as opposed to diathermy, certainly in the "doubtful" cases. Mr. Swan had raised the question of putting a catheter in the ureter. He (the President) did this as a routine, when possible, with the cystoscope, before opening the bladder. In some cases the growth overshadowed the ureter, and then it was not worth while wasting time in trying to find it.

Another point was the use of diathermy for diagnosis. Mr. Loughnane, raising the same point, had said that he diathermized these growths, and if they were not malignant he found that the mucous membrane healed afterwards, and one could tell which were innocent and which were malignant. [Mr. LOUGHNANE: If the mucous membrane heals you are dealing with a simple growth, but if there remain ulceration it ceases to be doubtful, it is malignant.] He agreed with that. But whether one was justified in using diathermy as a clinical test was not clear, and it meant loss of time. It was safer to excise doubtful ones.

Mr. Riches had quoted cases not properly within the scope of the discussion, that was to say, inoperable cases. These might well form the subject of discussion on another occasion. The same criticism applied to the remarks of Mr. Zachary Cope. Diathermy, radium, and deep X-ray therapy all had their place, but the present discussion was on operable cases.

Section of Pathology.

President—Professor E. H. KETTLE, M.D.

[*October* 12, 1920.]

PRESIDENT'S ADDRESS.

The Relation of Dust to Infection.

By E. H. KETTLE, M.D.

DUSTS of various kinds occur in the atmosphere in all parts of the world, and the inhalation of these dusts over periods of years inevitably produces changes in the lungs. Everyone is familiar with the pigmented lung of the city dweller, an example of a pathological change produced by the inhalation of dust which is of no clinical importance whatever, but an exaggeration of this condition in the coal-miner causes definite symptoms, and when the inhaled dust is not the relatively harmless carbon, but one of much more sinister possibilities, serious pulmonary changes develop. The pneumonoconioses have received less attention than they deserve, even in textbooks of medicine and pathology. But to the doctors whose patients are exposed to dusty trades, to those responsible for the conduct of these trades, and to the factory inspector, pneumonoconiosis is of great moment.

The Position in South Africa.—The disease in its most concentrated form is best seen in the gold-mining industry of South Africa, and it is difficult for anyone who has not actually visited the Rand to appreciate how large a place silicosis takes in the life of the mining population. I have been told that after the South African War, when it was desired to resume mining, search was made for experienced miners, but few were forthcoming. Some had returned to Cornwall, some had taken to other occupations, but the majority had died of miner's phthisis. Nowadays things are different. The would-be miner has to undergo a rigorous medical examination and none but picked men are accepted for employment underground. Periodical medical examinations are enforced, so that the disease is detected in its earliest stage, and everything that skill can do and money provide has been done to make the working conditions as healthy as possible. The incidence of pneumonoconiosis has been cut down a good deal, but it still exists, and since it is a disease which develops slowly, it is not easy to determine how efficacious modern methods of prevention are. There are now employed on the Rand some 15,000 white miners and about 150,000 natives. The wages bill is about 14½ million pounds a year, of which the Europeans, including surface workers, absorb about £8,000,000. In the last twenty years £12,000,000 have been paid in compensation to silicotics, mostly Europeans, and their widows and children. Every year between £800,000 and £1,000,000 are paid in compensation, and the industry is further faced with outstanding liabilities in respect of miners who may be expected to develop the disease, which are variously estimated at 6-11 million pounds.

These figures speak for themselves, but from another point of view the importance with which silicosis is regarded in South Africa is shown by the fact that since 1911 ten select Committees of the Legislature and five Commissions

have considered the matter, and nine Miners' Phthisis Acts have passed through Parliament.

The Position in Great Britain.—In Great Britain the dust risks are shared among a number of industries in different parts of the country. Excluding coal-miners, some 35,000 workers are employed in the refractories industry, tin mining, the pottery industry, metal grinding, sandstone working, sand blasting and other trades in which dust is a prominent feature. In these scattered industries it is difficult to arrive at comprehensive morbidity and mortality figures. On the Rand, with a localized industry, the registration and medical examination of the workers is as nearly perfect as it can be, but in this country the medical organization of the industries is nothing like so highly developed, and accurate statistics are difficult to obtain. It has been common knowledge for years that these trades are dangerous, but the first scheme of compensation for silicosis only came into operation in 1919, and there can be no doubt that industrial pulmonary disease will bulk much more largely in our social and medical legislation in the near future. Roughly speaking, the trades I have mentioned employ twice as many Europeans as do the Rand mines, and if we include, as we must, an unknown proportion of the huge population of coal-miners, the question becomes a very serious one.

In different occupations the composition of the dust will vary, but all dangerous dusts have one factor in common: they all contain free silica, the dioxide of silicon; and so far as we know the degree of harmfulness of a dust depends upon the amount of free silica present in it. It is quite true that certain silicates—asbestos is a notable example—in which silicon is present as a complex chemical substance are harmful to a certain degree, but they have not been studied in great detail, and for the present we may regard silica as the chief offender. Moreover, although the pulmonary disability induced by the different dusts has received various names, such as miner's phthisis, potter's asthma, grinder's rot, chalicosis, siderosis, the terminal pathological condition is always the same, and the victims die with advanced pulmonary tuberculosis. It is true that dust, and dust alone, may produce disability and death, and there is no doubt that it has done so in the past both in this country and in South Africa. But under modern social and industrial conditions dust disease, or silicosis, really spells tuberculosis; in fact, tuberculosis is recognized as the indicator of a dangerous dust. As pathologists, therefore, we are confronted with two main problems. First, how does silica affect the lung, and how may its action be prevented or modified; and secondly, how does it influence the development of pulmonary tuberculosis. In practice these problems are closely associated, but it is essential to make some attempt to separate them.

How does silica affect the lung?—The lung in uncomplicated silicosis presents a variable picture, but the characteristic feature consists of the presence in the lung substance of isolated nodules of fibrous tissue. They vary in size, number and distribution. In advanced cases a considerable proportion of the lung tissue may be destroyed, with consequent severe respiratory embarrassment. This massive fibrosis, however, is rarely seen nowadays; usually tuberculosis supervenes as a frank, or possibly a modified, infection. Now, in most forms of chronic fibrosis we are able to give some reasonable account of the development and progress of the lesion. By a histological analysis of, say, the various stages of the contracted granular kidney, we can describe pretty well how the condition is produced, but we have a good deal to learn about the development of the pulmonary lesions in silicosis. Until comparatively recently it was generally held that silicosis owed its harmful properties to its physical characters. The hard, sharp particles were supposed to damage the pulmonary tissue, and the whole process was regarded as a kind of microscopic trauma. For some years now, however, the view that silica becomes soluble in the tissues, and that its action is chemical rather than physical, has become generally accepted; and at the International Silicosis Conference held

this summer in South Africa, which I was privileged to attend as the representative of the Medical Research Council, it was agreed that "there is experimental evidence that the solubility of silica in the tissues is an essential factor in the causation of silicosis." It is also generally accepted that dust inhaled into the terminal alveoli is phagocyted by the pulmonary macrophages and transported to various parts of the lung. Presumably the silica gradually becomes dissolved, and in its soluble state is able to stimulate the growth of fibrous tissue. One cannot fail to be impressed by the difference in behaviour of quartz when it is introduced into the lung by way of the air passages, and when it is introduced directly into the tissues by subcutaneous inoculation. In the one case it is ingested by phagocytes, which may remain quiescent in the pulmonary alveoli for long periods of time without any signs of tissue reaction (fig. 1, p. 82); in the other, necrosis of the tissue takes place within hours or days, and there is an active inflammatory reaction (fig. 2). Presumably fibrosis can only occur if silica is brought into direct contact with fibrous tissue, or cells capable of forming it, and it has been suggested that the silicotic nodules start in the small areas of lymphoid tissue scattered throughout the lung, into which the phagocytes migrate. Certainly in experimental animals I have found a definite proliferation of the reticulum in the tracheo-bronchial lymph nodes, in which the dust cells have settled. But the various stages in the development of pulmonary silicosis have not, in my opinion, been fully worked out. It should not be a very difficult matter to obtain specimens of the disease in all its phases, and it is merely a question of careful and detailed histological analysis.

Experimental investigations might have been expected to help in the elucidation of the process, but for the most part they have not done much to clear the air, and this is not for want of time or trouble. I believe that the first money granted by the Medical Research Council was for an investigation into pneumonoconiosis, and work has been carried on continuously in this country and in South Africa ever since. Unfortunately, however, the investigations have not been devoted to the solution of the basal problems, but have largely been directed to the elucidation of subsidiary matters which seemed of more immediate importance; and the methods employed have not been adequate to solve the problem. L. U. Gardner, of the Trudeau Sanatorium at Saranac Lake, has realized that silicosis is a chronic disease which takes years to develop. He has, therefore, exposed his animals to dusty atmospheres for eight hours a day over periods of two to three years, and he has obtained most important results. But most other workers have been content with a total dust exposure of twenty-four to thirty-six hours, and I am not convinced that they have ever produced specific fibrosis; certainly they have produced nothing comparable with what occurs in man.

But it is in the more complicated forms of the disease that experimental investigation is most needed. Silica in harmful dusts is always associated with other substances, and the way in which these adulterant dusts may modify the main process can only be studied experimentally. From the statistics of certain dusty trades it would appear that, although the workers are exposed to a high percentage of silica, they do not suffer from silicosis. But statistics, unless they represent not only the truth, but the whole truth, may lead us seriously astray. To take one or two examples: it has often been stated that there is no silicosis in the mines of Mysore in India and Cripple Creek in U.S.A., though in both districts dust samples of the vein and the country rock contain a considerable quantity of free silica. Consequently, it has been taught that the adulterant dusts in these regions prevent the accumulation of silica in the lungs, and the corollary has been drawn that free silica does not necessarily mean silicosis. As a matter of fact, it emerged at the recent International Silicosis Conference that there is plenty of silicosis at Cripple Creek; and as regards Mysore accurate information is lacking.

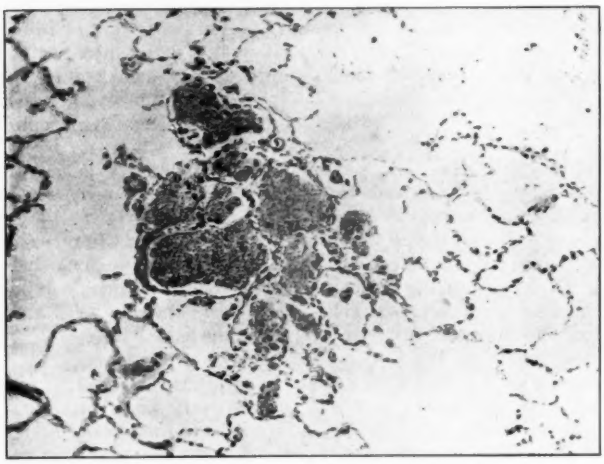

FIG. 1.—Section from the lung of a rabbit which had been exposed to a heavy atmosphere of siliceous dust during 33 hours a week for 18 weeks. Killed two weeks after the last exposure. Showing accumulation of dust cells in the lung alveoli but no fibrosis.

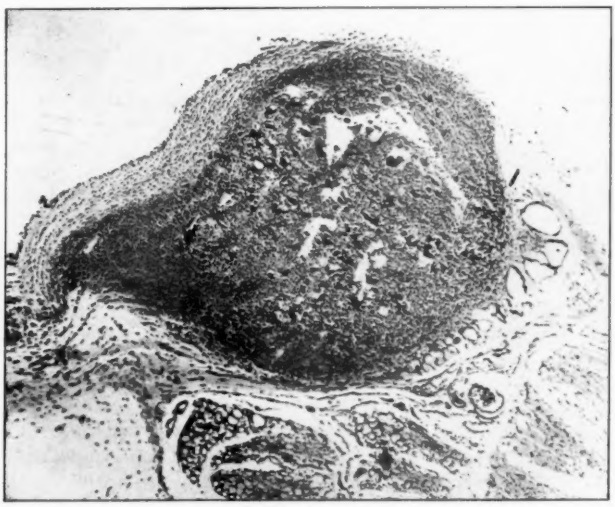

FIG. 2.—Section of the lesion produced in the subcutaneous tissue of a mouse by the injection of 1 c.c. of a 1% suspension of the same dust, showing the massive necrosis of tissue with secondary inflammatory reaction which proceeds to fibrosis.

We do not know whether there is any silicosis there or not. Again, the incidence of tuberculosis in dusty trades is adopted as the measure of the degree of silicosis present. Since the incidence of tuberculosis in coal-miners as a whole is actually less than in the general population, it has been believed that no silicosis occurs among them, though they are freely exposed to shale dust, which contains some 35% of quartz, and many of them actually have to drill through "hard headings" composed of rock with a high silica content. This anomaly again has been explained on the assumption that the adulterant dust (in this case coal) removes silica from the lung. But in fact it is not necessary to search for an explanation, because we now know that silicosis does occur in coal-miners (S. L. Cummins and A. F. Sladden [1]), at any rate among the men who work at hard headings, and the so-called anthracosis of coal-miners is probably silicosis affecting an anthracotic lung. N. Tattersall has dealt with this subject from the clinical point of view. He writes [2] :—

"Some three and one half years ago, accompanied by Professor Cummins, I visited a hard heading at Glyncorrwg. Two shifts of men were being used to drive a heading through some 300 yards of hard rock—three men boring on each shift. The dust was intense, so thick that one could see only about a yard when drilling was in progress. One of the men recognized me and I found out that he was a man I had recently examined and who was probably tuberculous, but at that time one sputum examination had been negative. About six months later I saw this man again, when he had marked signs and numerous tubercle bacilli in the sputum. He had been working all along in the same heading, coughing and spitting out tubercle bacilli. He died about a year later, the first of these six men to succumb; the sixth and last of them died two and one half years later from silicosis and tuberculosis."

Whatever may be the explanation of the relative immunity of the coal-miner to tuberculosis—if, indeed, such immunity really exists, and E. L. Collis [3] points out that it certainly does not apply to the whole body of coal-miners—it cannot be the absence of silicosis. Can it be due to the actual presence of the coal dust? Coal dust itself is a complex substance and varies in composition, but all coals consist largely of carbon; is carbon therefore antagonistic to the tubercle bacillus? Carleton [4] suggests that "it is conceivable that pulmonary tuberculosis might favourably respond to a carefully graded inhalation of coal or soot particles," but I should imagine that the failure of this form of therapy is being demonstrated daily among the consumptives of our great cities. I know of no experimental evidence to support this view, and moreover I have not been able to demonstrate any difference from the normal, in their reaction to the tubercle bacillus, of animals saturated with carbon in attempts to block the reticulo-endothelial system.

The demonstration of silicosis among coal-miners is of such importance because a whole superstructure of theory has been built up on the assumption that it does not exist. From observations in man and in experimental animals we know that when coal is inhaled into the lung it is picked up by phagocytes. By the migration of these phagocytes much of the dust is removed, either by way of the air passages or by the lymphatics. If the quantity of dust inhaled is great, intake will overcome excretion and coal will remain in the lung. Much of it is deposited in lymphatic vessels, but from the fact that a miner's sputum is pigmented for a long time after he ceases work, it would seem that a good deal still remains in the alveoli. The pigmented lung of the city dweller suggests that the excretion is never perfect, but yet it has been claimed that small quantities of coal may entirely disappear from the lungs of experimental animals by this natural method of cleansing. Dr. J. S. Haldane [5] suggests that the capacity for getting rid of dust can be greatly increased by use, and he also says that to excite such a physiological process as elimination of dust particles some stimulus is needed. Within limits this is no doubt true, but I cannot follow him when he says that such a stimulus cannot be supplied by crystalline dust, but only by non-crystalline dust. Whereas coal is held to

provide all the stimulation necessary, he regards silica as incapable of providing this stimulus owing to its "inertness, impenetrability and insolubility"; one would have said that these qualities really belong to coal rather than to silica. He believes that the coal-miner is free from silicosis because the inert silica is carried away by phagocytes stimulated by the coal. In a more recent paper Haldane [6] says that to stimulate phagocytes a dust must be itself soluble or contain something soluble. Coal and other protective dusts are more or less amorphous and consequently porous. They therefore contain impurities which may be soluble. Apart from this, amorphous substances are naturally less insoluble than crystalline substances, from the looser aggregation of their molecules. This conception has been supported by experiments which have been freely quoted. Carleton [4] exposed animals to a mixture of coal and flint, and states that the brisk phagocytosis initiated by the coal dust was responsible for the rapid elimination of much of the flint from the lungs; but from the descriptions and illustrations given in this paper there seems to be little difference between the lungs of these animals and those of others which had been dusted with flint alone. Mavrogordato [7], again, in 1922 reported experiments in which three groups of guinea-pigs were dusted with (*a*) silica alone; (*b*) silica followed by coal, and (*c*) silica preceded by coal. After six months the lungs of the animals in group (*a*) were found to be grey, those in group (*b*) black, and those in group (*c*) white. Although a considerable quantity of silica could be detected microscopically in group (*c*), the other two groups contained far more. In a communication made to the International Silicosis Conference this year, however, reviewing all his experiments, he says that previous invasion by coal does not appreciably hinder the settlement of silica in the lungs. One set of conclusions appears to cancel out the other. But neither Carleton's nor Mavrogordato's experiments really answer the question. Recognizable specific lesions were not produced in the control animals dusted with silica alone, and there is no evidence that in these experiments the coal either helps or hinders the action of the silica.

Intra-tracheal Injections.—During the last year Dr. R. Hilton and I have attempted to take a short cut by introducing suspensions of dust directly into the lungs of rabbits and guinea-pigs. We have found this a comparatively simple procedure. Under urethane anæsthesia a small nick is made in the skin on the front of the neck, the trachea is localized and the needle of a record syringe introduced into it. Guinea-pigs tolerate anything up to 2 c.c. of dust suspension and rabbits 5 c.c. or more. The experiments are, of course, excessively artificial, but provided not too much is claimed from them, they should be capable of giving useful information; and, as a matter of fact, even in the usual dusting experiments, there is not much real resemblance between the miner, the potter, and the stone mason employed on their lawful occasions, and the rabbit or guinea-pig in the dusting chamber. Our results have been rather disappointing. We felt that our technique was open to the criticism that a single flooding of the lung with an overwhelming dose of dust can have no relation to the continuous inhalation of small quantities, and consequently that silicosis produced in this way would not be comparable with the disease in man. But, so far, we have not even been able to produce the typical fibrosis, and since an adequate quantity of dust must have been introduced into the lung, it is clear that the time factor is of the first importance.

In one series of experiments, 5 c.c. of a 2% suspension of dust from a South African mine in distilled water was inoculated intra-tracheally into a series of rabbits. Two doses were given, on the first and sixty-third day of the experiment. Figs. 3 and 4 are taken from the lung of a rabbit killed thirty-six days after the second inoculation. There is practically no free or phagocyted dust in the alveoli; it has all been transported into the lymphatics, which in places are widely distended. Some of the dust appears to be free, but a good deal is still contained within phagocytes. In the area illustrated the lung is contracted and puckered,

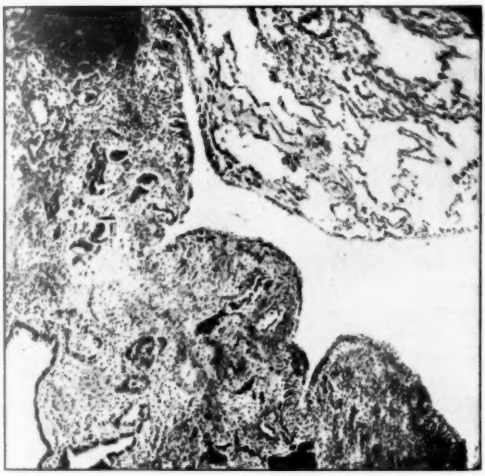

FIG. 3.—Section of the lung of a rabbit which had received two intra-tracheal injections of mine dust (Modder E. gold mine) on the first and sixty-third day of the experiment—killed on the ninety-ninth day, showing puckering and apparent fibrosis of the lung.

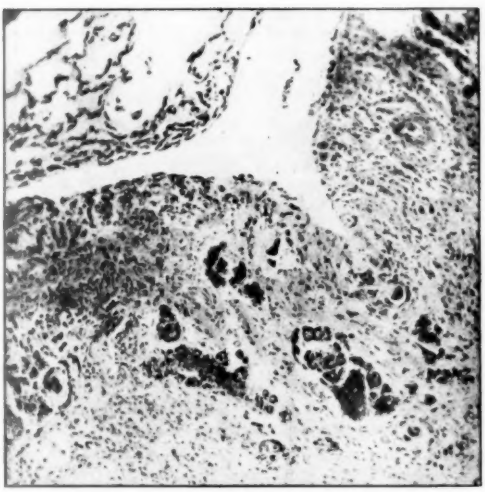

FIG. 4.—Higher-power photograph of fig. 3 showing masses of dust in the lymphatics with condensation of the surrounding lung.

and the alveolar structure destroyed. In the affected areas there is an increase of fibrous tissue, but it suggests to me the condensation associated with atelectasis rather than true fibrosis, and this opinion is borne out by the appearance shown in fig. 5. This is a section of the lung of an animal in the same series, killed ninety-two days after the second dose, but no more fibrosis has developed. In places I have thought it possible to distinguish the deposits from the first and second inoculations from the difference in size of the particles, but this is the only sign of solution I have found.

Fig. 6 shows the lung of a guinea-pig killed on the two hundred and fifth day after a single intra-tracheal injection of mine dust. In guinea-pigs we have not found the same rapid determination of dust to the lymphatics, and in this lung much of the dust is still in the alveoli.

Great stress has been laid on the immobilization of phagocytes by silica, and Mavrogordato [7] suggests that it mummifies them, preserving them in much the same way as water glass preserves eggs. It would seem more likely that retention of silica in the lung depends upon the destruction of phagocytes rather than their preservation, but however that may be, retention is the essential factor. A harmful dust is said to be one which is not eliminated from the lung, and the contrast is always drawn between silica and the stimulating carbon which is readily removed from the lung by a process of natural cleansing. Gardner, on the other hand, states that quartz produces the greatest degree of phagocytic activity of any dust he has investigated, and suggests that immobilization of phagocytes in the lung depends upon the load they have ingested. He finds no evidence that silica preserves cells better than any other kind of dust.

Further experiments which Hilton and I have carried out have a bearing on this point. Fig. 7 (p. 88) is taken from the lung of a rabbit, which received two intra-tracheal doses of carbon in the form of dilute indian ink at an interval of fifty-eight days; it was killed one hundred and forty-seven days after the last injection. Here carbon particles are still present in the alveoli, and the appearances closely resemble those seen in fig. 6. The heavily pigmented mine dust and the carbon both tend to obscure cell outlines, and it is difficult to make out the details, but there seems to be no essential difference between the initial reaction and subsequent behaviour of the phagocytes when carbon is used instead of mine dust. Fig. 8, taken from another part of the same lung, shows the subpleural deposition of carbon, exactly comparable with what one constantly sees in human material. Even making allowance for the initial heavy dose, there does not seem to have been a very pronounced migration of carbon from the lung, and I conclude that the amount of carbon or other dust which remains after dusting is in direct ratio to the thoroughness of the exposure.

We have varied these experiments, using mixtures of amorphous silica and carbon, and mine dust and carbon, but with the technique we have employed we have seen no sign of the characteristic cleansing which has been described.

I have confined my remarks to coal dust because this is the adulterant dust most often quoted, but I have no reason to believe that other concomitant dusts in industries play any specific part in protecting the individual from the effects of inhaled silica. The experiments which have been accepted in the past as having significance are not capable of giving the answer required. We must have a base-line to work on, and in these experiments the base-line must be the production of characteristic silicosis in animals. In the absence of this we are not justified in claiming experimental knowledge of how silicosis may be modified.

So far I have only discussed the protective adulterant dusts, but there is another side of the question, for it is possible that these concomitants may actually assist the action of silica. Of recent years attention has been directed to the occurrence of silicosis in the manufacture of certain abrasive powders. In one factory in which an abrasive powder, consisting of silica 75% and sodium carbonate and powdered soap 25% was prepared, several cases of acute silicosis have been described, following comparatively brief exposures to the dust. Two of the fatal cases were described in the *Lancet* [8] recently, and though in one of them it is recorded that tubercle

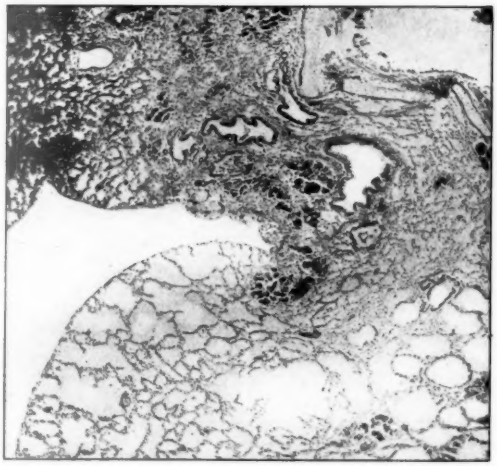

FIG. 5.—Section of the lung from another rabbit of the experiment illustrated in fig. 3, in this case killed on the 155th day. There is no essential difference in the lungs of the two animals.

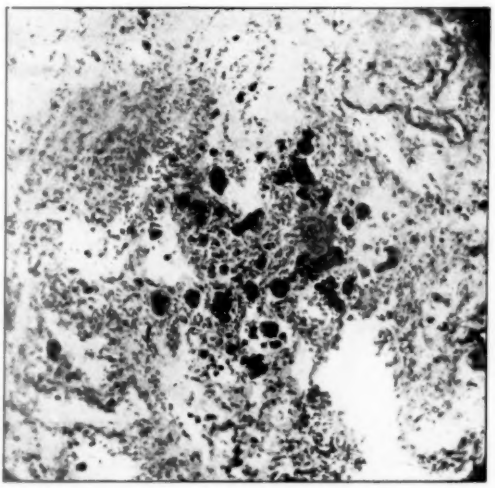

FIG. 6.—Section of the lung of a guinea-pig killed 205 days after a single intra-tracheal injection of mine dust (Modder E.). The dust is mainly in phagocytes which are lying free in the alveoli. There is no fibrosis.

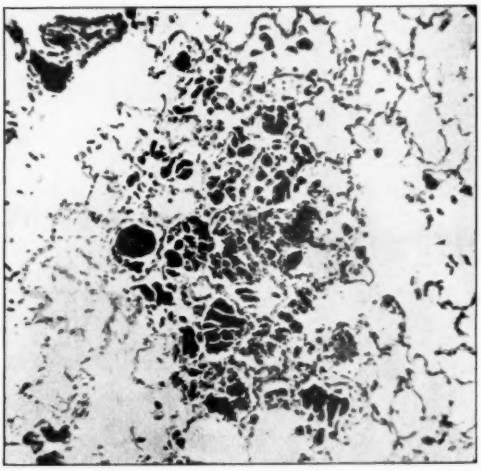

FIG. 7.—Section of the lung of a rabbit which received two intra-tracheal injections of carbon (Higgins indian ink 1 in 5 normal saline) at 58 days' interval—killed 147 days after the second injection. The carbon is lying free and in phagocytes in the lung alveoli.

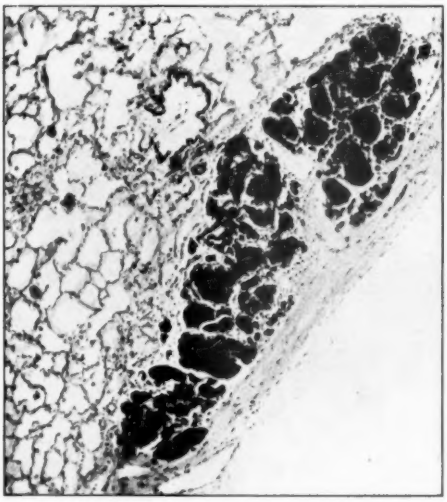

FIG. 8.—Another part of the same lung illustrated in fig. 7. Here the carbon has been transported to the subpleural lymphatics where it has accumulated and is producing slight fibrosis. This is exactly comparable with what occurs frequently in man.

bacilli were present in the lungs, the infective element is evidently regarded by the authors as being quite unimportant. It is known that silica is soluble in alkaline solutions, and the explanation given for the rapid onset of the disease is that the inhaled alkali increases the solubility of the silica and enables it to act much more rapidly than usual. There is an unfortunate tendency, when considering the solubility of inhaled dusts, to forget that we are dealing with a complicated anatomical structure, and to regard the lungs as a couple of test tubes in which all sorts of chemical reactions can take place unhindered. In the paper referred to, it is assumed that several chemical reactions occur with quite a complex geological formation as the end-product. It may, of course, be so, but even then there is no adequate explanation of the subsequent fibrosis. I have, as a matter of fact, been privileged to examine portions of the lung from one of the cases, and also the lungs from another fatal case occurring in the same factory, and in neither of them have I found the changes described, though in one of them there is undoubtedly nodular fibrosis. On the other hand, I have found advanced tuberculosis in both cases, and this I regard as the basis of the whole condition. It is more than likely that the infection was enhanced by the inhaled silica, but it cannot be claimed that there is evidence in the lesions of the pure adjuvant action of an adulterant dust. In view of these cases I have also carried out a few dusting experiments, but I have not been able so far to demonstrate any difference between the changes produced by the inhalation of pure amorphous silica and of the same dust mixed with sodium carbonate.

The effect of silica on pulmonary tuberculosis.—This brings me to the second question, the effect of silica on pulmonary tuberculosis. Silica, as I have said, may itself produce profound changes in the lungs, but nowadays industries are so controlled that workers are rarely, as it were, choked with dust. They inhale a certain amount of silica which may produce a fairly advanced fibrosis of the lung, but the chief danger lies in the influence the dust exercises on microbic infection. Simple bronchitis is a recognized complication of dusty trades, and there is evidence that other respiratory infections may be increased by silica, but the one infection which stands out above all others is tuberculosis, and the great problem in the pneumonoconioses is the relation of the dust to the tubercle bacillus. There is abundant clinical evidence that silica has a specific action on the growth of the bacillus, and experimental work in the last few years has done much to clarify our conceptions of the process. It was formerly supposed that it was the fibrosis induced by the silica that in some way or another predisposed the lung to tuberculosis, presumably from interference with lymphatic drainage, although this was not clearly stated. Haldane [5] wrote in 1924: "We can easily imagine how a lung that becomes more and more clogged with dust should also become more and more susceptible to the attacks of the tubercle bacillus." But he distinguishes between various forms of pneumonoconiosis and suggests that the fibrotic change due to a relatively harmless dust is of much less significance than a similar change brought about by a dangerous sort of dust. It would be truer to say, I think, that the fibrosis has no significance at all, and that the only thing that matters is the nature of the dust.

No experiments have been carried out in this country on the infection of the fibrotic lung, but fairly extensive observations have been made on the effects exercised by silica on tuberculosis in laboratory animals. Some years ago Gye and I [9] demonstrated that interstitial inoculation of different forms of silica produced characteristic necrotic lesions, and that tubercle bacilli proliferated readily in these lesions in such insusceptible animals as mice. Later, I was able to show that the active growth of the bacilli did not depend merely on the necrosis of the tissue, but was due to the actual presence of the silica [10]. Further experiments confirm this view. If particulate silica is inoculated intravenously into rabbits it is picked up by macrophages in, especially, the liver, spleen and lung. If

the dose has not been too heavy, many of these cells remain capable of function, and may be expected to ingest other foreign particles free in the blood-stream. Having prepared animals in this way, I then subjected them to an intravenous inoculation with living tubercle bacilli, and killed them at varying intervals of time. The protocol of such an experiment is shown in fig. 9. Very often there is no significant difference between the treated and the control animals, which is what one would expect, for it is largely a matter of chance whether one kills the animals at the most appropriate time. If one kills them too soon the bacilli will not have had time to proliferate; if too late the effect of the silica, which is only present in small quantities, will be obscured by the natural reaction between the host and the organism Nevertheless, I think I have been able to demonstrate in the majority of my experiments that it is possible to modify an artificial miliary tuberculosis by silica. Fig. 10 is taken from the lung of a rabbit, which received during nine days eight intravenous doses of amorphous silica (1 c.c. of a 1% solution). On the eleventh day it was inoculated intravenously with living tubercle bacilli, and it was killed eleven days later. Fig. 11 is taken from the lung of the control animal, which was inoculated with a similar dose of bacilli without previous treatment. There is a very definite difference in the number and size of the lesions in the two animals.

Figs. 12 and 13 are taken from the lungs of the treated and control animal of another series. Four preliminary doses of silica were given during ten days, and the animal was killed twelve days after infection. (See fig. 9.) In this experiment the macroscropic difference in the tuberculization of the lungs is not so obvious, but fig. 14 shows the much greater number of bacilli in the lesions of the silica animal as compared with the control (fig. 15).

Fig. 16 is taken from a section of the lung of a rabbit inoculated intra-tracheally with a suspension of tubercle bacilli to which mine dust has been added, and killed eight days later. The control animal (fig. 17) received the same number of bacilli in the same volume of fluid, but no mine dust, and again the difference in the number of bacilli in the two animals is pronounced. There can be no question of necrosis here; the bacilli are not growing in a pabulum of necrotic protoplasm, but in phagocytes which are healthy enough to ingest them. I do not wish to lay too much stress on these experiments, for they contain sources of error. For example, it is an extremely difficult thing to give exactly similar doses of living tubercle bacilli to a considerable quantity of animals. But they all point in the same direction, and I think they are significant. Hilton and I have also carried out a limited number of experiments, in which guinea-pigs and rabbits received intra-tracheal injections of silica, and some weeks later were inoculated intra-tracheally, together with an adequate number of controls, with living tubercle bacilli. All the animals died with pulmonary tuberculosis, but the silica animals died weeks, or even months, before the controls. These experiments again are suggestive, but I am not prepared to say more than that.

L. U. Gardner [11], however, has performed an experiment which seems to me to be crucial. They have at Saranac a strain of tubercle bacilli, R1, which produces in guinea-pigs infected by inhalation, isolated subpleural nodules in the lung, and massive involvement of the tracheo-bronchial glands. Macroscopic tubercles in other viscera practically never occur. The pulmonary lesions caseate in four to six weeks, but the bacilli then die off and healing by resolution takes place in eighteen months to two years. The lymph nodes also heal, but may show some residual fibrosis. The infection is practically never fatal. Animals infected with this bacillus are dusted with quartz for eight hours a day over a period of two to three years. After three to five months the bacilli in the pulmonary lesions take on a new capacity for growth. The process spreads to all parts of the lung, massive ulcerative lesions occur, and the infection extends to the abdomen. This change is

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PLATE I.

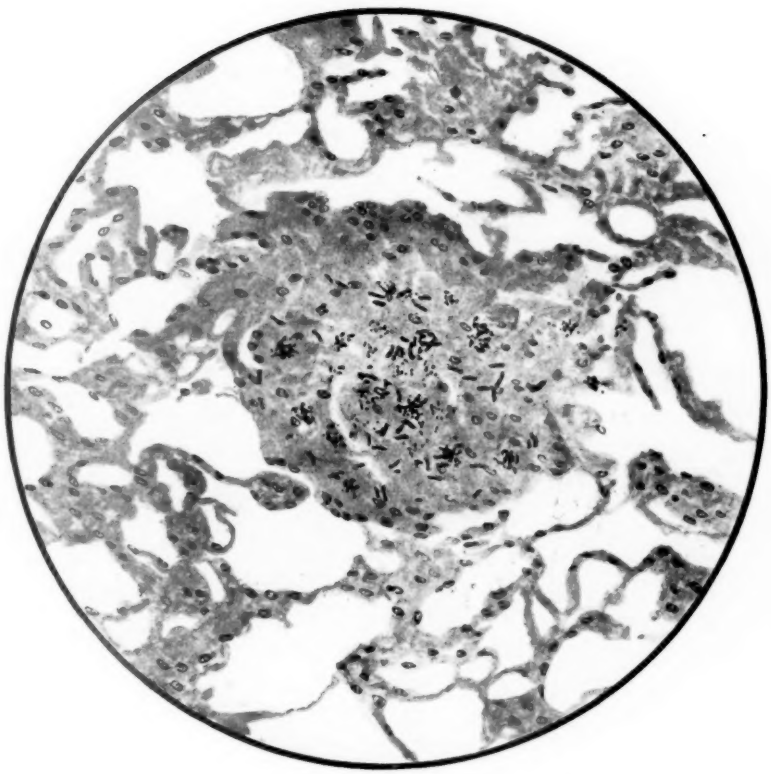

FIG. 14.—High-power view of a lesion in the lung of rabbit 2—(fig. 12)—showing large number of tubercle bacilli.

PLATE II.

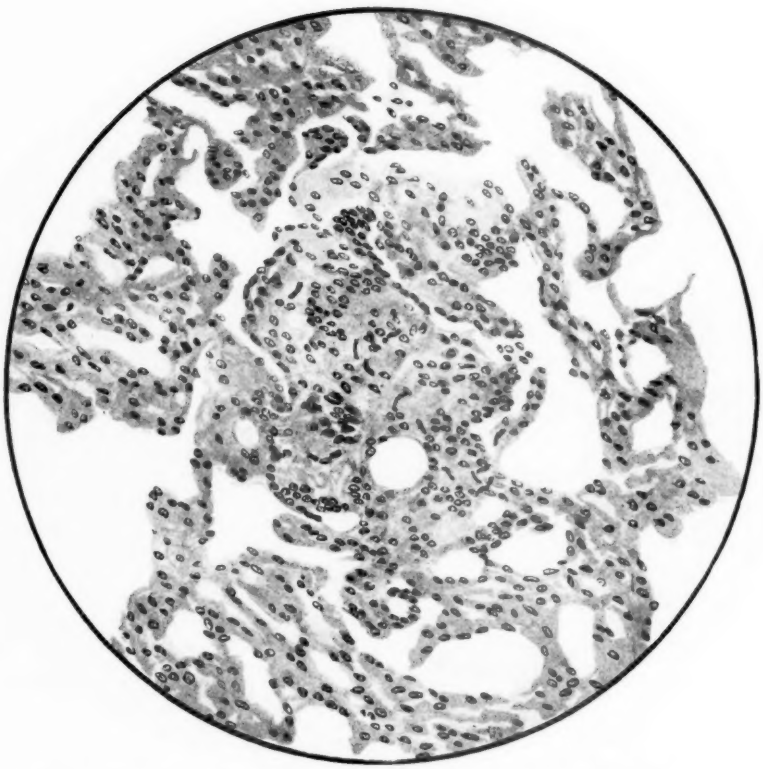

FIG. 15.—High-power view of a lesion in the lung of rabbit 8—(fig. 13)—very few tubercle bacilli.

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PLATE III.

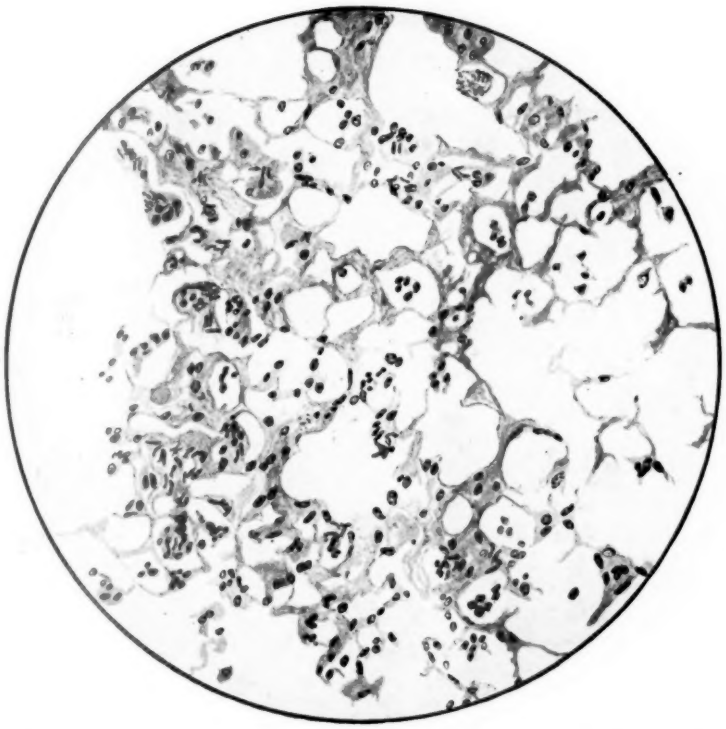

FIG. 16.—High-power view of lung of a rabbit which had received an intratracheal inoculation of tubercle bacilli together with mine dust. Killed eight days later.

PLATE IV.

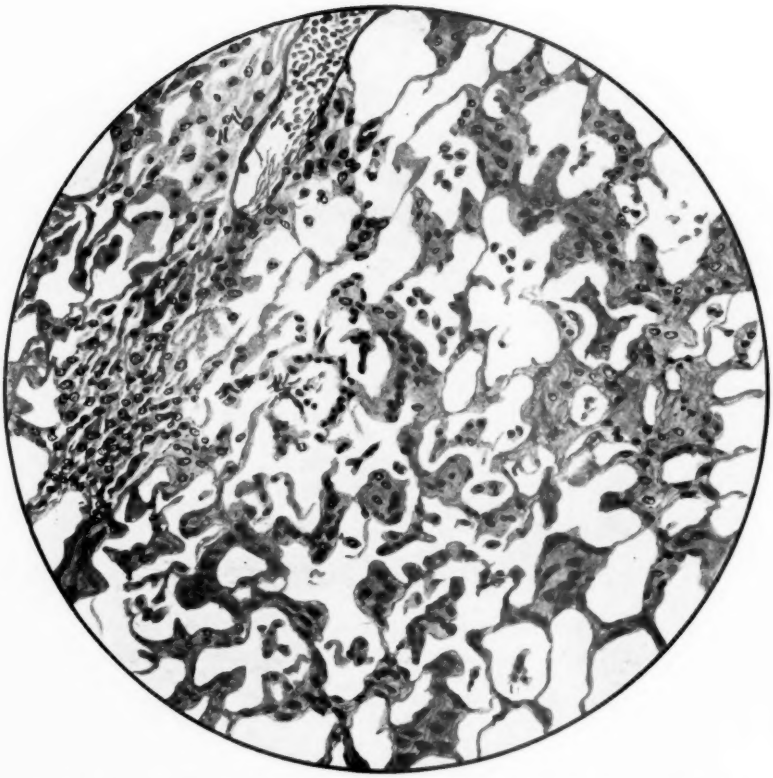

FIG. 17.—High-power view of lung of a rabbit, control to the one illustrated in fig. 16. It had received tubercle bacilli intratracheally but no mine dust. Note the difference in the proliferation of the bacilli.

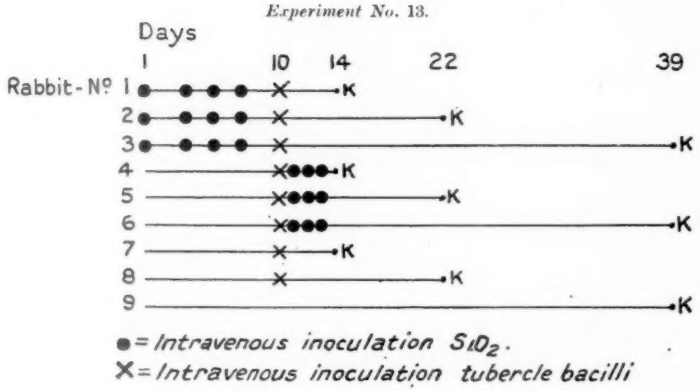

FIG. 9.—Protocol of experiment showing the modification of an artificial miliary tuberculosis by silica.

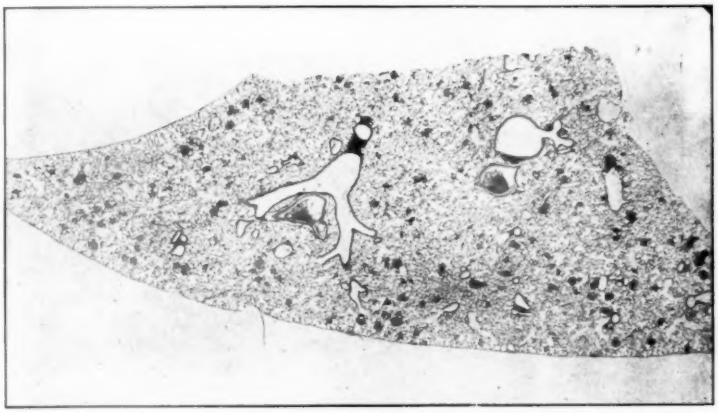

FIG. 10.—Low-power view of lung of a rabbit which had received eight intravenous inoculations of amorphous silica in nine days—on the eleventh day it was inoculated intravenously with living tubercle bacilli and was killed on the twenty-second day. Note the considerable number of miliary tubercles.

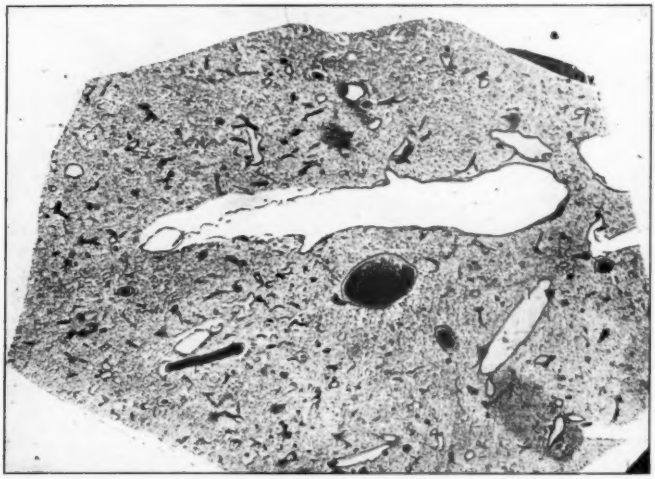

FIG. 11.—Section of the lung of the control animal in the experiment illustrated in fig. 10. It received tubercle bacilli without previous treatment with silica—there are very few miliary tubercles.

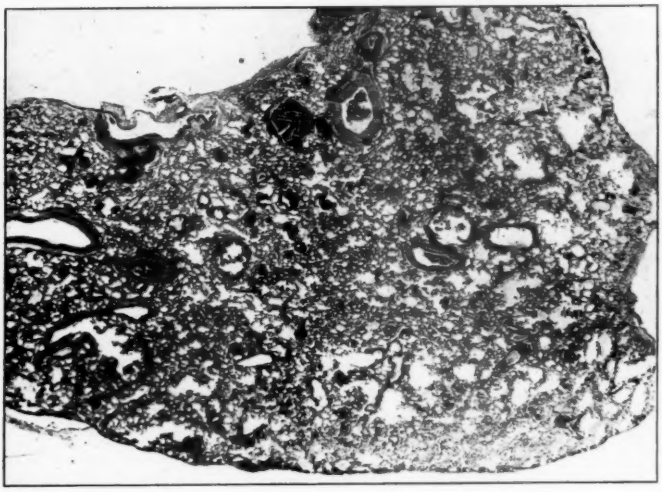

FIG. 12.—Section of lung of rabbit 2—fig. 9.

not due to an exaltation of the virulence of the bacilli, for subinoculations from the animals produce merely the form of tuberculosis characteristic of the R1 strain. It appears to be due to an alteration of environment, due to the presence of the silica.

Exactly how the silica acts is still doubtful. Cummins [12] suggests that it destroys complement; but to me the phenomenon appears to be a cellular rather than a humoral one. Either the intracellular defensive mechanism of the phagocyte is injured by the silica, or the nutritional value of the cell protoplasm for the bacillus is enhanced. I have attempted to bring about the same kind of thing *in vitro* by the addition of silica to culture media, and Dr. L. P. Garrod is working on that side of the matter with me now. I have found in some experiments that, although the total growth of the bacillus is unaffected, the lag period seems to be shortened, so that an abundant growth is obtained in a much shorter time when silica is added to the medium than when it is absent. Gardner reports

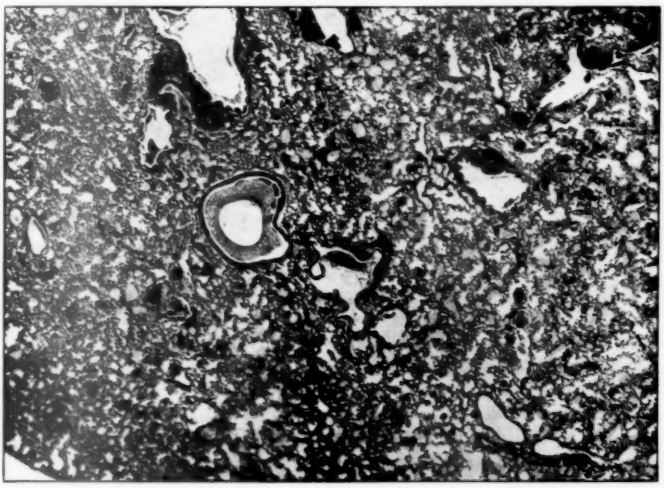

FIG. 13.—Section of lung of rabbit 8—fig. 9. In the lungs the macroscopic tuberculization is about the same in the two animals.

the same kind of results. But these experiments are very irregular. They may come off once, and the next time may be a complete failure, and so far I am not prepared to say that any success I have had is more than accidental. *In vivo*, however, I do not think there can be any doubt about the main facts, though the explanation is still to seek.

Infective silicosis.—I have left one other aspect of the silica problem to the last because in some ways it is the most difficult of all. In South Africa they recognize simple silicosis and silicosis with tuberculosis, or tuberculo-silicosis. In addition, they describe another condition, infective silicosis, in which infection is believed to produce changes in the reaction of the tissues to the dust. The actual nature of the infection has not been determined in every case, but the tubercle bacillus is thought to be by far the most important organism. I believe I am right in saying that infective silicosis was the most troublesome subject discussed at the recent conference in South Africa. In the first place it seemed to me that the visiting delegates as a whole were unacquainted with this condition, and found it difficult to

understand the conception of the process accepted in South Africa; and secondly, it seems to involve a complete change in our views of the action of silica on tuberculous infections.

In this form of the disease radiographic examinations reveal a form of fibrosis in which the individual nodules are larger and more irregular in outline than in typical simple silicosis, and tend to coalesce in areas with a somewhat diffuse formation of fibrous tissue; and on naked-eye and microscopic examination the nodules appear to differ from the true silicotic nodules chiefly in the direction of a greater tendency to necrosis. The cases tend to pursue a chronic course, and the lesions show no histological evidence of tuberculosis such as occurs when infection becomes grafted on to a silicotic lung. Even when these nodules develop as the result of a combined action of the bacillus and the dust from the very earliest stages, the typical tuberculous reaction is absent. How then, one may ask, is it possible to say that the tubercle bacillus plays any part in the process, for apparently it has not been demonstrated in the lesion? The answer is that while the nodules of simple silicosis inoculated into guinea-pigs do not produce tuberculosis, nodules from cases of "infective silicosis" give positive results, though, from the lesions produced, the bacillus appears to be of an attenuated type. Only a few cases have as yet been available for biological tests, but the investigations are being pursued. In the discussions at the recent conference the suggestion was made by South African workers that silica may actually damage the bacillus so as to lower its virulence, and this was regarded as the explanation of the process. And it was definitely laid down that [13]: ". . . in many cases of clinically 'simple silicosis,' even at its earliest detectable stage, an element of low grade and latent tuberculous infection may already be present in association with certain of the 'silicotic' lesions." It is difficult to reconcile this view with the available experimental data. All the evidence goes to show that the influence of silica on the tubercle bacillus is always favourable to the bacillus. And I find it equally difficult to visualize a process in which the silica crystal and the tubercle bacillus, acting simultaneously, can produce a fibrotic lesion which will limit the action of the bacillus by encapsulation. However, opinion among South African workers is very firm that such an infective silicosis does occur, and their experience is so great and they have achieved so much in the study and prevention of miner's phthisis, that their views must carry great weight. I think we must accept the existence of such a modified form of silicosis, and direct our attention to its further investigation.

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Section of Dermatology.

President—Dr. S. Ernest Dore.

[*October* 16, 1930.]

Mycosis Fungoides.—J. E. M. Wigley, M.B.

Female, aged 73. Recurrent attacks of eczema for many years. These have never quite cleared away. The tumours have only been present a few weeks. She presents numerous tender tumours on both buttocks, on the right leg, on the abdominal wall below the umbilicus, in the left axilla, on the right wrist, and over the cervical vertebræ. There is also a widely scattered eruption, made up of slightly indurated "eczematous" patches. The whole of the skin is pigmented, and suggests a pruritic eruption of long standing. The itching complained of is moderate. Histological section of one of the "eczematous" patches showed the typical polymorphous cellular infiltration of the corium. Treatment by X-rays has diminished the size of the tumours considerably.

Exfoliative Dermatitis associated with Rheumatoid Arthritis.—J. E. M. Wigley, M.B.

Male, aged 52, first seen at St. John's Hospital, September 5, 1930. His skin was then almost universally red, exfoliating in large flakes, and without any sign of weeping areas; he was feeling the cold very much. The small joints of his hands were deformed, as in rheumatoid arthritis. He has improved greatly with rest in bed and iodine internally. He says that his skin has been affected for two years, and his joints for eighteen months. When previously under Dr. Barber he had psoriasis, and gave a history of previous attacks of exfoliative dermatitis. The eruption now is very suggestive of psoriasis. Pathological investigations have proved uniformly negative.

Discussion.—Dr. F. Parkes Weber said he did not think Sir Archibald Garrod and Dr. G. Evans, in their article on "Arthropathia Psoriatica" in the *Quarterly Journal of Medicine* (1924, xvii, p. 171), mentioned any case which presented such generalized exfoliative dermatitis as this present patient did.

Dr. H. MacCormac said he had at the present time in his ward a female patient with exfoliative dermatitis following psoriasis—her second attack of this condition. On the first occasion progressive joint changes had developed; these subsided when the eruption improved, and a similar association of joint and skin changes was again observed.

The President said it was difficult to say whether the joint changes with which dermatologists were familiar in psoriasis were ætiologically associated with that disease. Sometimes they preceded the skin condition and sometimes occurred later in the course of the disease. In his experience the terminal phalangeal joints were those most commonly affected. With regard to the comparatively frequent occurrence of exfoliative dermatitis following psoriasis, it was possible that these cases might be really instances of severe generalized psoriasis.

Urticaria Pigmentosa in an Adult.—F. Parkes Weber, M.D.

The patient, Mrs. E. B., aged 26 years, is shown as a characteristic example of urticaria pigmentosa in an adult. The skin of her whole body and limbs is studded with brown macules, on the average about 3 mm. to 5 mm. in diameter (see figure, p. 2). In other respects she appears normal and healthy, excepting that the differential count of her white blood-cells gives 38% lymphocytes. Wassermann reaction, negative. The macules (which first began to appear when she was 21 years old and have not

been increasing in number for some time) are not elevated and cannot be distinguished from the rest of the skin by feeling them. But on being rubbed they become bright red and elevated (that is to say, they become turgid), and then commence to itch. If

Urticaria pigmentosa.

left to themselves the swelling and the red coloration and itching soon disappear. Apart from this there is no urticaria factitia or dermographia, and apparently there is no tendency to spontaneous urticaria.

Telangiectasia Macularis Eruptiva Perstans—probably a telangiectatic variety of urticaria pigmentosa in an adult.—F. PARKES WEBER, M.D.

A somewhat obese woman, Mrs. F. N., aged 60, has, since the age of 40, or earlier, developed a most striking condition of generalized cutaneous macular telangiectasia, which has now become quiescent. The persistent red macules are distributed chiefly over the upper part of the front of the thorax, the outer surfaces of the upper limbs and the abdomen. They are, therefore, by no means confined to exposed surfaces, and that speaks against a traumatic element in the ætiology. There is no special evidence in favour of a neuropathic ætiology. The face is free from macules, though it presents many linear arborescent telangiectases of the ordinary kind. There are no purpuric lesions anywhere. The presence of brownish pigmentation in some of the lesions is quite unmistakable (with or even without diascopic pressure); the lesions become redder and some of them become definitely elevated (or *more* elevated) on rubbing them, though this is not associated with any itching. Slight factitious urticaria can be produced over the back of the thorax. I suggest that the case is an extremely rare telangiectatic and relatively pigmentless variety of urticaria pigmentosa in an adult.

For full discussion of the case, with illustrations, see F. Parkes Weber and R. Hellenschmied, *Brit. Journ. Derm. and Syph.*, 1930, xlii, 374-382. Dr. Weber believes that a case of this kind has never previously been regarded as a variety of urticaria pigmentosa. Such a diagnosis was not hinted at by Colcott Fox when he quoted cases of the kind in the *Brit. Journ. Dermat.*, 1908, xx, 154-156; but E. Besnier seems to have thought that E. Vidal's case (a woman, aged 31) might be related to urticaria (*Bull. de la Soc. méd. des Hôpitaux de Paris*, 1880, 2nd series, xvii, 186-188). The cases described by Sir William Osler as "Telangiectasis

Circumscripta Universalis" (*Johns Hopkins Hosp. Bull.*, 1907, xviii, 401) were evidently of the same class.

Discussion.—The PRESIDENT said he wished to protest against adding a new name to the already overburdened nomenclature of dermatology. He did not know whether this condition had been described under this name before. [Dr. WEBER: I have simplified it; it is a descriptive name.][1] With regard to the presence of telangiectasia in Dr. Weber's case he thought they were present in other parts although not in the eruptive lesion. He thought Dr. Colcott Fox's paper mainly referred to cases of familial telangiectasis.

Dr. GRAHAM LITTLE said he hoped the Section would not encourage the re-labelling of known diseases with new names. One would have taken this for a condition with which dermatologists were familiar, though it was rare, i.e., urticaria pigmentosa in an adult. He was referring to both cases shown by Dr. Parkes Weber; he did not think that the second could properly be so sharply differentiated from the first as Dr. Parkes Weber supposed. The lesions on the forearm of the second case were of the same type as those in the first case and in his (the speaker's) own case which he would presently discuss. A more important feature of differentiation was the presence or absence of mast cells. There was, he submitted, a well recognized group of adult urticaria pigmentosa, and Dr. Weber's case came into that.

Dr. H. CORSI said it was unfortunate that the name mentioned was so long, as it was liable to bring dermatologists into derision with members of other branches of the profession. It was, however, a better name than urticaria pigmentosa. Darier, in his textbook, placed urticaria pigmentosa among the naevi, and then telangiectasia was a more suitable name. In his own case of urticaria pigmentosa a section was examined, and Professor Kettle, without having seen the patient, reported that he thought it was lymphangioma, as telangiectases were visible in the section; he was uncertain whether they were capillaries or lymph vessels; on the whole, however, he thought they were lymph vessels. There were no mast cells; this, some might say, put it out of the category of urticaria pigmentosa. There seemed to be a few telangiectatic blood-vessels visible, and that clinical fact would again bring the case into line with Dr. Parkes Weber's telangiectasia.

Dr. G. B. DOWLING asked whether the telangiectases in the second case were to be seen on or among the lesions of urticaria pigmentosa or were they on the face only? He did not think that any special significance should be attached to dilated vessels on the face occurring after the menopause; and suggested that they might be unrelated to the urticaria pigmentosa.

Dr. PARKES WEBER said that the typical telangiectases in his second case were on the face only.

Dr. H. MACCORMAC said that he remembered Dr. Colcott Fox's paper, but his impression was that it referred to a family type and to a form with a tendency to hæmorrhages from the nasal mucosa. The confusion with syphilis mentioned reminded him that it had been stated that in some cases of adult urticaria pigmentosa the Wassermann reaction was positive: this he had also observed in two patients under his care.

Dr. A. C. ROXBURGH said that the late Dr. Maurice Hannay had published in the *British Journal of Dermatology* about 1924 a paper on a number of cases of urticaria pigmentosa, and had concluded that mast cells were commonly absent in adult cases, and that only in juvenile cases were they constantly met with.

Alopecia Totalis in a Young Woman.—F. PARKES WEBER, M.D.

The patient (A.B.), aged 23 years, is an unmarried woman, born in England of Continental Jewish parents. She appears to be physically and mentally normal, excepting in regard to her hair and a somewhat infantile condition of the internal sexual organs, as far as can be judged by examination per rectum. She is said to be of a very "nervous" disposition. She is bald (see fig.), without eyelashes and eyebrows and with very scanty axillary and hardly any pubic hair. There is practically no "lanugo" hair over the glabrous parts of the body (a little on right leg and right fingers). There is no evidence of thyroidal abnormality, and by X-ray

[1] Dr. Weber's was more descriptive than L. Brocq's term, *Télangiectasies essentielles en plaques acquises*, and than similar terms quoted under Colcott Fox's subheading "Essential Telangiectases in Plaques." Some other dermatologists in London were not sure that Dr. Weber was right in regarding the second case as a variety of urticaria pigmentosa.—F. P. W.

examination the pituitary fossa appears to be of normal size and shape. No abnormality of nails or teeth. She sweats normally.

The history is that on the whole she has enjoyed good health. As far back as she can remember there was a small bald patch in the centre at the back of the top of her head. At 14 years of age she had one menstrual period, but none further until the age of 17 years. Since then menstruation has been fairly regular, but very scanty. At 15 years of age she is said to have had a "nervous breakdown,"—possibly of hysterical nature. At 17½ years (a few months after the commencement of regular menstruation) all the hair of her scalp and eyebrows, and her eyelashes, fell out within one month. At about 19½ years of age a little hair grew again on her scalp—

Alopecia totalis.

possibly as a result of some kind of treatment—but fell out again after three or four months. There is no family history of any similar condition.

I am inclined to regard this and some similar cases of "acquired" alopecia totalis as due to an inherent congenital potential weakness in hair-growth, so that a physical or psychical shock or an endocrine disturbance is sufficient completely to extinguish growth or make it "flicker" before finally extinguishing it. The patient thinks that intermittent courses of the application of a formalin solution to the scalp have caused slight improvement, but this is certainly not striking. There are probably various groups of "acquired" alopecia totalis of somewhat different (though unknown) causation.

Alopecia Totalis in a Boy after Slight Nervous Shock.—F. PARKES WEBER, M.D.

Shown for comparison with the preceding case. This case was described in detail in *Proc. Roy. Soc. Med.* (Section for the Study of Disease in Children, 1929-1930, xxiii, 56).

Dr. W. KENNETH WILLS said he had had two cases which came to him on the same day. One was that of a female patient whom he had seen ten years previously because of universal

alopecia. Treatment was unsuccessful. On this occasion she came to show that her hair had grown normally after she had passed the climacteric.

The second case was that of a patient who, having reached the climacteric, had lost all her hair. She regained her hair on being treated by the administration of ovarian substance.

Another case was that of a man aged 60, who had no hair on his head, and whose scalp was affected by a seborrhœide. There were no follicles distinguishable by means of a lens. Under local treatment a thick thatch of black hair returned.

There seemed to be at least two reasons for alopecia; some cases were related to endocrine disturbance, while others were not.

Leucoderma, *vel* Leucotrichia.—S. ERNEST DORE, M.D. (President).

Patient, male, aged 20. His hair began to grow white in patches when he was 9 years old. There are now numerous patches of white hair on the scalp and the chin. The eyebrows and eyelashes are similarly affected; the axillary hair is partly white on both sides, the lower part being pigmented. On the legs there are also patches of leucotrichia, and the hair, as in other parts, appears to be more scanty than the pigmented hair surrounding it. The pubic hair is completely white. The patient's paternal grandmother is stated to have had white hair at the age of 21.

Dr. Roxburgh considers that the leucoderma is more apparent than real, and that it would be more appropriate to describe the condition as leucotrichia.

Lichen (?). Case for Diagnosis.—KNOWSLEY SIBLEY, M.D.

P. W., single, healthy-looking girl, aged 21. Machinist. No history of skin trouble in her family; father living and well; mother died from cancer at the age of 41. She herself has always had good health.

The present skin eruption commenced some two years ago, with a single spot on the left leg, then others appeared on the left wrist and elbow, and these have gradually increased until there are now from 20 to 30 of these spots scattered irregularly, chiefly on the arms and legs, but there are also a few on the posterior part of the neck. She says that they begin as minute, dull white papules slightly irritable on or before eruption, then becoming rather red, and finally atrophic, and leaving small pearly white, slightly depressed scars with a reddish margin, which apparently remain permanently.

Most of the spots are circular, but a few are eccentric or irregular in outline. Lesions are absent from the buccal mucosa.

Biopsy (Dr. Muende).—"Beyond the existence of a deep-seated fatty nodule, no pathological lesion could be found. Collagen and elastic tissue were normal."

The following diagnoses have been suggested: (1) Anetodermia; (2) Lichen atrophicus; (3) Pityriasis lichenoides et varioliforma acuta; (4) Tuberculide.

Dr. BARBER said that an identical case had been shown at Copenhagen, but he did not remember what was the diagnosis. In that case, however, there were more lesions than in this one. He regarded the present case as one of lichen planus atrophicus.

Lichen Planus with Unusual Features.—E. G. GRAHAM LITTLE, M.D.

The patient is a man, aged 50.

Both palms are studded with acuminate papules, grouped together and forming a fairly hard mass, and occupying the whole palm. It has persisted unchanged for twenty years, during which time it has been treated by many methods, including X-ray therapy, but without improvement. In addition there is a typical lichen planus of the mucosa of the mouth and a ringed lichen planus of the glans penis.

Dr. DOUGLAS HEATH said that when the hands and feet were involved in long-standing cases of lichen planus there was a condition like keratosis punctata, and the patient now shown had that appearance. It appeared to be very intractable. In the case of a man who was constantly using tools, the chance of alleviating the condition was not great.

One did not now see much secondary syphilis of the palm. In the case of two dentists who had accidentally acquired syphilis some years ago, the palmar lesions were much aggravated by the use of the dental forceps; such dentists had come to him because of raised, cracking lesions on the palms of the hands, which caused great discomfort.

Lesions (? Psoriatic) on Palms. Case for Diagnosis.—E. G. GRAHAM LITTLE, M.D.

This patient, aged 24, entered a motor car works as an advisory engineer, and in the course of his occupation he handled gritty oils. Six months after commencing this work he began to get hard "calluses" on his palms; these were very painful and bled freely. I saw him last January and he improved under treatment and absence from the work. Since January he has been doing a another kind of work. As he is a brilliant science student, the motor-car firm are keeping the post open for him. The moment he comes into contact with anything hard he gets these lesions, which some Members suggest may be psoriatic, and the reaction is extraordinarily rapid. For instance, I suggested to him that instead of using his palm he should, when possible, use the ball of his thumb, but a lesion has developed at the point when he has done this. To-day both palms are studded with these lesions. Is the condition psoriasis, or is it a curious vulnerability to callosity formation? He had small, indefinite lesions of psoriasis on his elbows, but nowhere else, and these have disappeared. Even along the line of contact with the forefinger when he holds the pen in writing, a similar lesion has developed, and when he shifts the pen to the middle finger the same thing happens at the new point of contact.

Dr. DOUGLAS HEATH said he thought that the condition was psoriasis of the hands. A more common form of psoriasis was that in which one could scrape out white silvery scales from little holes in the palm. These were embedded in the thick skin. In the case of people who used tools there occurred a flatter form of lesion, with keratosis on the surface, and plaques might form and coalesce. He had seen cases in which the whole palm was occupied by a sheet-like form of psoriasis, which yielded to anti-psoriasis treatment. Sometimes, as in the present case, it was associated with a few lesions elsewhere.

Urticaria Pigmentosa in an Adult.—E. G. GRAHAM LITTLE, M.D.

Patient, male, aged 42. The condition has persisted since he was 12 years old. I have sections showing mast-celled formation. Juvenile urticaria pigmentosa usually vanishes at puberty. In the paper I wrote in 1908 I described the case of a boy who was almost covered with the eruption, yet when I saw him twenty years later he had no lesions whatever of that character.

Leucotrichia with Leucoderma and Melanoderma.—E. G. GRAHAM LITTLE, M.D.

Patient, female, aged 40. Leucoderma and melanoderma of the body recently developed, also a leucodermic patch involving the entire scalp and to about half an inch beyond the hairy part. The hair is dead-white but quite thick, though without any pigment, and the de-pigmentation extends for about half an inch beyond the region of the hairy scalp, which is thus wholly surrounded with a narrow, white margin.

Herpes Gestationis.—E. G. GRAHAM LITTLE, M.D.

This condition, in my experience, is very rare. The patient, a woman aged 35, who has been twice pregnant before, the two children having been born without involvement of the mother's skin during or after pregnancy. She is now eight months pregnant, and the rash appeared three weeks ago as a typical dermatitis herpetiformis eruption on the forearms, arms, etc.

Trichophytia Profunda.—E. G. GRAHAM LITTLE, M.D.

This case was brought up by a naval surgeon from Chatham. The patient is a soldier who, in 1926, was in China. On the way home some scaly and scabbed lesions developed on the nape of the neck. In June, 1929, blisters began to appear in both armpits; several coalesced to form a large blister the size of a five-shilling piece, leaving a raw surface. These cleared from the axillæ in a few weeks, but recurred in December, 1929, and have remained practically the same ever since. The groins are similarly affected. In July, 1930, curious lesions began to appear on his scalp, large granulomatous patches, obviously consisting of suppuration round hair follicles, forming a boggy mass. I think the condition is a ringworm granuloma; we found plentiful mycelium in the feet this morning, but we did not find any in the hair, which we are testing with culture media. Pemphigus vegetans might be suggested by the history, and that was the naval surgeon's diagnosis; the masses on the scalp have been regarded as tertiary syphilis, but repeated Wassermann tests performed at Chatham have proved negative.

Lupus Erythematosus of the Erythema Migrans Type.—W. N. GOLDSMITH, M.D. (for Dr. A. M. H. GRAY).

A. H., female, aged 36, first attended University College Hospital in July, 1929. For thirteen years she had had a recurrent eruption on the face and, more recently, on the fingers. Condition in July, 1929: Ringed erythematous non-atrophic lesions on right cheek and on tip of nose, where there was also rather thick scaling. Tips of fingers showed atrophy and telangiectasis, and on the back of the fingers were pin-head telangiectases at a distance from the atrophic part. Patient was treated at first with quinine and soon after with triphal. The eruption, however, became a little more flushed and painful, and figurate lesions with wheal-like edges appeared on that part of the chest exposed to the sun. There was then a temporary improvement, but new lesions soon appeared on the arms and legs in spite of the continuation of triphal injections. Tuberculin tests (intradermic) performed early in 1930; reactions were negative on two occasions. Treatment was continued with lopion, but the patient continued to grow worse, the finger-tips being especially painful for the few days preceding the monthly periods. Examination of the nose and throat revealed no focus of infection. In May, 1930, the patient was admitted to the ward after severe bleeding from the rectum and general malaise. No rectal disease was found. A radiogram of the chest gave evidence of old healed tuberculosis. At this time she had large ringed infiltrated lesions on the right arm. In August, 1930, intradermic tests were performed with tuberculin, *Streptococcus hæmolyticus* and *viridans* and *Staphylococcus pyogenes aureus*. None were positive. Autohæmotherapy (two injections) was followed by the development of further lesions on the face. There are now ringed lesions on each side of the nose, below each ear and on the left arm, and there is characteristic scaling on the tip of the nose. The tips of the fingers are telangiectatic and atrophic and on the back of them are numerous angiokeratomas. The feet are similarly affected. Quite recently large spontaneous "bruises" have appeared on the lower limbs.

Summary.—This is a severe example of the erythema migrans type of lupus erythematosus. The ringed lesions with raised edges do not "migrate" much. They start as rings and spread very slowly outwards, leaving no atrophy. No active pyococcal or tuberculous focus has been found, and all intradermic tests are negative. Light plays a definite provocative rôle on the face and chest, but lesions appear on covered parts, such as the arm, as well. The patient has not been benefited by any of the treatments so far given. There is clearly some potent poison attacking the blood-vessels.

Pseudo-pelade of Brocq.—H. CORSI, F.R.C.S.

R. S., male, aged 37, a Pole, arrived in England fifteen years ago. He then had a fine head of hair, as shown by a photograph taken at that time.

During the past eleven years small spots of baldness have appeared from time to time; the hair has never grown on these places again.

In addition there is a good deal of ordinary baldness and in this the cicatricial process of the pseudo-pelade is particularly well seen.

Urticaria Pigmentosa.—H. CORSI, F.R.C.S.

E. P., female, aged 24, married.

A rash first appeared on the face when she was aged 17, and gradually spread over the greater part of the body. It is now most marked on face, breasts, legs, forearms and hands.

It consists of spots of discoloration—pink, violet, red-brown or cayenne pepper. On vitro-pressure the pink spots disappear. When the spots are rubbed, or when the patient has a hot bath, they become urticarial, but they do not itch.

Histological report.—There is a proliferation of the capillaries or lymphatics. No pigment can be seen. Mast cells were not found.

Atrophic Lesions on Joints of Hands and Feet. Case for Diagnosis.—G. B. DOWLING, M.D.

I brought this case up because the condition is rare. The patient, a girl aged 20, has had the condition practically from birth, and a sister has had an exactly similar condition; it is therefore familial and congenital. The lesions are situated on the dorsal aspects of the interphalangeal joints of the feet and hands, and on the metacarpo-phalangeal joints of the hands. They consist of circumscribed patches of atrophy, red in colour, with scattered dilated capillaries. The patches feel like parchment. By putting the skin on the back of the hand on the stretch, one can see numerous tiny atrophic striæ. There is thus an extension of the process to the skin of the whole hand, though nothing abnormal would be noticed without close observation.

It is evidently a developmental malformation, but I have not seen the condition before.

Discussion.—Dr. F. PARKES WEBER thought the case should be called one of *congenital cutaneous defects* (because one ought not to be sure that the lesion was merely ectodermal), of the same nature as I. A. Abt's "congenital skin defects" (*Amer. Journ. Dis. Child.*, 1917, xiv, p. 113). He was interested in the familial feature.

Dr. A. M. H. GRAY said he did not see this case, but some years ago he showed a child who had an atrophic lesion on the wrist, with telangiectases.[1] There were also other nævoid lesions on the body. These congenital aplastic lesions must be very rare.

1 *Proceedings*, 1925, xviii (Sect. Derm., 9).

Section of Anæsthetics.

President—Dr. H. W. FEATHERSTONE.

[*November* 7, 1930.]

PRESIDENT'S ADDRESS.

[ABRIDGED]

A Visit to Some of the Hospitals in Canada and to the Mayo Clinic.

By H. W. FEATHERSTONE, M.D.

DURING the last ten years several papers have been read before this Section, dealing with the practice of anæsthesia in Canada and in the United States of America. Dr. Boyle and Dr. Mennell have given us the benefit of their experience in those countries, and their observations and their criticisms were, in each case, backed by a ripe experience and enriched by a trenchant wit which I envy but which I cannot emulate.

This summer I visited Quebec, Montreal, Niagara, Toronto, Winnipeg and Rochester, and came home through Chicago, Philadelphia and New York. No words of mine can do justice to the cheerful welcome and the open-handed hospitality accorded to us wherever we went.

Dr. Apperly and I together saw something of anæsthetic practice in Montreal, Toronto, and Winnipeg. Dr. Apperly inspected Ottawa, and Dr. Magill, Dr. Parsons and I visited Winnipeg and the Mayo Clinic.

When visiting the Montreal General Hospital, we first encountered certain variations in technique which, though new and unaccustomed in our experience, we found were commonly employed in the clinics which we visited.

(1) *Premedication.*—At Montreal, Toronto and Winnipeg, atropine is rarely given before anæsthesia. We formed the opinion that the employment of morphine and scopolamine with much nitrous oxide and very little ether in a dry climate, enabled our colleagues to dispense with the use of atropine. In Stewart's practice, morphine is given in two small doses one hour and a half and half an hour respectively, before the operation. 1/150 gr. of scopolamine is given with the second dose of morphine. After the first dose of morphine the patient is kept absolutely quiet, and encouraged not to speak.

(2) *Nitrous oxide-oxygen* is used in large amounts in all these clinics, and, in my experience, ether is added rather liberally. The cost of nitrous oxide is about the same as in London; 3,200 gallons of nitrous oxide, to fill one of the great gas cylinders on the McKesson Trolley, cost about £12, and last about a fortnight in the ordinary run of work.

(3) *Ethylene* is not used very much in Montreal and Toronto. Johnston and Shields of Toronto, and Stewart of Montreal, stated that it was too readily exploded. A case was cited in which a man was anæsthetized with ethylene and oxygen. Diathermy of the mouth was decided upon, so that a change was made to gas-oxygen for ten minutes and then the diathermy electrode was applied. An

explosion followed, which killed the patient and injured the medical attendants. It was supposed that in this case some ethylene and oxygen had been swallowed during the induction of anæsthesia, and that the patient regurgitated the explosive gases when the diathermy was commenced.

Lundy, at the Mayo Clinic, said that he liked both ethylene and acetylene, the latter especially for thoracic work. He had records of 39,000 administrations of ethylene without an accident. At Winnipeg ethylene is used widely.

For my part, I dislike the absence of a margin of safety. In the literature of these explosions (and it is quite considerable) death of the patient from rupture of the lung has been the inevitable result of an explosion.

(4) *Sodium Amytal* is receiving a great deal of attention. It is employed as a basal anæsthetic in a manner similar to that of avertin; it is used as a hypnotic and has been valuable in non-surgical conditions. It may be administered by the mouth, by the rectum, or intravenously. The intra-venous route has proved valuable because the dosage can be controlled accurately.

From six to fifteen grains of the white powder, sodium iso-amyl-ethyl barbiturate, are dissolved in about 10 c.c. of distilled water. The solution must be quite clear, and the injection should be made at a rate not exceeding one grain of the drug per minute, that is to say a ten-grain dose should take ten minutes to inject. Rapid injection produces sudden and dangerous fall in systolic blood-pressure, and œdema of the lungs may occur. For the treatment of pulmonary œdema, the intravenous injection of a 50% solution of glucose, the injection of atropine, and the administration of oxygen are recommended.

The effect of the drug is extremely rapid, and rhythmical breathing, with drowsiness and sleep, takes place in a few minutes after the commencement of the injection. Excitement may occur, but this is more likely during the recovery. We found that opinions with regard to dosage varied. Stewart used about fifteen grains, the Toronto school employed from six to thirteen grains, Zerfas of Indianapolis had used as much as forty-five grains (about three grams). Lundy, at the Mayo Clinic, found that from six to fifteen grains intra-venously caused hypnosis, and from fifteen to thirty grains produced anæsthesia. Nitrous-oxide-oxygen is given during the operation when only hypnosis has occurred. Recovery is slow, and with a large dose of fifteen grains, twenty-four hours may elapse before the patient is fully conscious. Lundy said: "Measure the induction in *minutes* per grain of the drug, and the recovery in *hours* per grain."

(5) *The employment of novocain crystals for spinal analgesia* was recommended at most clinics.

From 0·15 to 0·25 gramme of novocain in sterile crystalline form is obtained in an ampoule; the ampoule is opened and the drip from a lumbar puncture is collected therein. The solution of novocain in cerebrospinal fluid is drawn up into a syringe and after the syringe has been inserted into the lumbar puncture needle, the novocain solution is diluted with cerebrospinal fluid to about 8 to 10 c.c. This solution is then injected.

For a high abdominal case ten c.c. of cerebrospinal fluid containing 0·25 gramme of novocain are used, but for the lower abdomen about 0·15 gramme in 6 c.c. of cerebrospinal fluid suffice. Upper abdominal cases are injected not lower than the first lumbar space. The patient is tilted head lowermost, not indeed to alter the level of the analgesia, but in order to counteract the fall in blood-pressure. Curiously enough I did not hear any references to the spinocain technique. Percain has not as yet received much attention. In Canada it is called nupercain.

(6) *Blood-pressure readings.*—Although continuous blood-pressure readings were taken in most of the clinics, an anæsthetist at Montreal was not convinced of their value and he put forward views which I think some of us in this country hold, namely, that they disturb the patient and distract the attention of the anæsthetist

and that when the patient is failing, the condition as seen clinically is more informative than the blood-pressure chart. In one or two cases I perceived an unsatisfactory condition of cyanosis in the arm below the bandage, which was due to negligence in not releasing the air from the armlet after the readings had been taken.

The main block of the Toronto General Hospital is a fine, well-equipped building, and some interesting cases were shown to us.

For the radical cure of a hernia a spinal anæsthetic was given. 150 mgm. of novocain crystals were dissolved in 6 c.c. cerebrospinal fluid preceded by morphine, hyoscine and atropine. The anæsthesia was excellent, and the anæsthetist said that in his experience headache was rare.

The new private patients' pavilion attached to this hospital merits a fuller description than I can give here. It is placed alongside the main hospital, and contains 330 beds arranged in separate rooms on eight floors, with eight or nine operating theatres on the ninth, i.e., the top, floor, and a magnificent kitchen occupies the basement. Most, if not all, of the bedrooms are single rooms, attractively furnished, and each has a private bathroom and toilet. The charges are from four to twelve dollars a day, including charges for meals and nursing service—that is to say, from £5 12s. to £17 a week.

At Winnipeg the Anæsthetic Section discussed intra-tracheal technique, avertin, post-operative pneumonia, anæsthesia for operations on the gravid uterus and the administration of the barbiturates (sodium amytal, embutal and pernokton). Dr. Magill's special rubber intra-tracheal tube for "blind" intubation through the nose excited much interest and admiration.

Dr. McKesson of Toledo, Dr. John Lundy, Chief Anæsthetist at the Mayo Clinic, Dr. Zerfas from Indianapolis, Dr. Walters from Madison, Wisconsin, Dr. Sam Johnston, and Dr. Shields from Toronto, Dr. Lamb from Glasgow, and doctors who hailed from India, South Africa, and many other parts of the British Empire, joined in the discussions. Dr. Apperly, the President of the Section, conveyed to those present the good wishes of the Section of Anæsthetics of the Royal Society of Medicine.

The great Annual Dinner of the Association was held in the Hudson Bay Company's store, and fifteen hundred people were present. The eloquent speech of Lord Moynihan in proposing the toast of "The British Empire" will live long in our memories, and Sir StClair Thomson's wit was received with tremendous appreciation. I was struck by Professor Chipman's remark: "Ladies and Gentlemen, we welcome you to the Golden West,—but it is only Golden when we have sold our grain!"

At the Mayo Clinic, each theatre was equipped with a huge Heidbrink machine for giving ethylene, nitrous-oxide, oxygen, and carbon dioxide. Lundy showed us a special machine made by the Heidbrink Company which incorporated acetylene and a carbon filter. Sodium amytal and embutal were employed in hypnotic doses. Dr. Balfour performed a partial gastrectomy under morphine, scopolamine, embutal, ethylene-oxygen (and perhaps a trace of ether). The ethylene-oxygen was administered by a nurse-anæsthetist, who took the blood-pressure at frequent intervals. High spinal anæsthesia for upper abdominal surgery was demonstrated.

Throughout our visit we were impressed by the sympathetic manner with which the patients were treated, while, at the same time, the patients permitted a free discussion of their conditions and of their prognoses without appearing at all concerned. It is this complete confidence and remarkable tolerance on the part of the patient which enable the surgeon in America to perform such extensive operations under local anæsthesia.

Lundy controls the Department of Anatomy, and his School of Local and Infiltration Anæsthesia, which is associated with the Anatomical Department, is remarkably instructive and complete.

Discussion.—Dr. F. B. PARSONS said that gaseous anæsthetics were employed to a far greater extent in Canada and the United States than in this country, and apparatus for their administration was constantly being improved. As an example of this, a McKesson machine was fitted with a device for graphically recording the pulse-rate, the respiration rate, and the amount of anæsthetic administered.

Mr. MAGILL said that he had visited the General Hospital at Winnipeg and had seen several anæsthetists at work. The McKesson machine was in general use and ethylene was employed when possible, with the addition of small amounts of ether when necessary. He was impressed with the results obtained with ethylene and felt compelled to alter his own previously expressed opinion that equal results could be obtained with nitrous oxide, oxygen and ether.

At the Mayo Clinic he was impressed with the efficiency of the nurse-anæsthetists. They were trained for a year under the senior anæsthetist before being permitted to undertake the administration of an anæsthetic unaided. Their practical experience would therefore bear more than favourable comparison with that of a newly qualified doctor in England.

It was apparent that Lundy's principle of "balanced anæsthesia" was the keynote of the work at this clinic. Premedication was carefully attended to, every effort being made to secure "sedation" before an operation. In this connection embutal was one of the most valuable agents in use as a basal anæsthetic.

In abdominal surgery there was an evident preference for spinal anæsthesia with novocain and the results obtained were impressive. Hiccough or nausea during spinal anæsthesia was treated with inhalations of carbon dioxide and oxygen.

It was particularly noted, both at Winnipeg and the Mayo Clinic, that cyanosis in any degree was not tolerated by surgeons or anæsthetists. When muscular relaxation under general anæsthesia was required, ethylene and oxygen were used, with the addition of ether when necessary.

Dr. H. P. FAIRLIE said that he was interested to hear how relatively small a place open ether now took in the anæsthetic practice across the Atlantic. When he visited the United States in 1907 it was practically the routine anæsthetic at a time when it was only beginning to be used in Great Britain. It was interesting also to hear Dr. Magill's favourable impression of ethylene. References in the trans-Atlantic journals to the preliminary administration of the barbituric acid derivatives, especially as to their value when given by mouth, seemed to open out hopeful possibilities.

Section for the Study of Disease in Children.

President—Dr. HUGH THURSFIELD.

[*October* 24, 1930.]

Lesion of Both Auditory Nerves, together with Several Other Cranial Nerves on the Left Side.—F. PARKES WEBER, M.D., and M. SCHOLTZ, M.D.

The patient, J. F., is a well-nourished girl, aged 12 years, with complete loss of function of both auditory nerves, including the vestibular portions, according to the caloric test (Dr. W. Wilson). Paresis of facial muscles and soft palate on left side. Left lingual hemi-atrophy, with fibrillary twitching. Left recurrent laryngeal paralysis. Slight indistinctness ("thickness") in speech. Sometimes slight dysphagia. No spinal accessory nerve involvement. Slight nystagmus on looking to the left. The patient frequently has headache over the right eyebrow and in the adjoining temporal region. No vertigo. No vomiting. Posterior polar cataract (congenital) in right eye. The optic discs have somewhat indistinct edges, but the presence of true papillœdema has been questioned. Dr. C. Markus, however (October 13), is definitely of opinion that there is bilateral papillœdema (the right optic disc can be seen in spite of the cataract). The right eye vision (owing to the cataract) is $\frac{3}{36}$; the left eye vision (with correcting lens) is $\frac{6}{12}$. The superficial abdominal reflexes seem to be absent on the left side, but can be sometimes obtained on the right side.

There are no other abnormal signs. Sensation apparently is unaffected. X-ray examination of the skull shows nothing pathological, though the pituitary fossa is rather large (deep). Gait normal. No Rombergism. No Babinski sign. Tendon reflexes normal. Blood-serum gives negative Wassermann and Meinicke reactions. No lumbar puncture made. No cutaneous neurofibromata or abnormal pigmentation.

History.—The deafness, now bilateral and complete, was first noted, on the left side only, about December, 1929. An alteration in the child's speech was remarked by the mother about March, 1930. About August, 1930, "twitching" on the left side of the tongue was observed, and the child complained of a feeling as if the food tended to "stick in her throat." There is a history of occasional slight epileptic seizures (sometimes in the night, sometimes in the day) since the age of 6½ years; one such attack whilst under observation in the German Hospital was limited to the right side, but that seems to have been exceptional. Otherwise, excepting for diphtheria at 3 years of age, nothing abnormal was observed previously to the present illness. No family history of importance. The mother has two other children, aged 8 and 16 years respectively; no children have died; no miscarriages.

In regard to *diagnosis* there are two suggestions:—

(1) Bilateral auditory nerve tumours (as pictured in Oppenheim's *Nervenkrankheiten*, seventh German edition, 1923, p. 1441, fig. 449), but on the left side the tumour (neurofibroma?) would have to be larger, or else, to account for the clinical signs, there would have to be more than one tumour involving different cranial nerves on the left side. (2) Syringobulbia.

We are much indebted to Dr. D. H. Brinton for information on the patient's condition at the National Hospital, Queen Square, where she was this year an in-patient under Dr. Gordon Holmes.

Intracranial Tumour.—H. E. MANSELL, B.M. (for Dr. DONALD PATERSON).

R. H., male, aged 3 years, who had previously seemed well, having had no illnesses of note, was seized three months ago with a fit, preceded by headache and vomiting for a few hours. He became unconscious and there were twitchings and convulsions severe enough to necessitate chloroform administration. In hospital no signs of organic disease were found and the patient was discharged after removal of septic tonsils. Walked at normal age but had never talked. The fit was considered to be epileptic and the child to be a mental defective. A month ago he was readmitted on account of another attack of headache and vomiting, followed this time by a squint and unsteadiness of gait.

On Examination: bilateral papillœdema. Pupils equal and react normally: weakness of left external rectus; doubtful weakness of right masseter; weakness of right lower facial muscles; palate and tongue normal; weakness and ataxy of right arm and leg, the gait being reeling with a tendency to fall to the right.

All tendon reflexes on right side exaggerated; feebly sustained right ankle clonus; plantar reflex doubtful; abdominal reflexes not elicited.

During past month physical signs and papillœdema have increased in spite of radium treatment. Opinions of Members of the Section are sought as to localization of tumour and advisability of decompression.

[A brief discussion on the advisability of decompression followed, in which Professor Vining inclined to non-interference. The majority of other speakers, however, considered that operation afforded the best chance of benefiting the patient.]

Two Cases of Associated Deformities of the Cranium and Extremities.—JEAN SMITH, M.D. (for Dr. ERIC PRITCHARD).

(I) Acrocephaly with Syndactyly.—R. S., female, aged 5 months. Head shows marked increase of vertical diameter due to extension upwards of cranial vault, highest point of which coincides with anterior fontanelle which is very tense

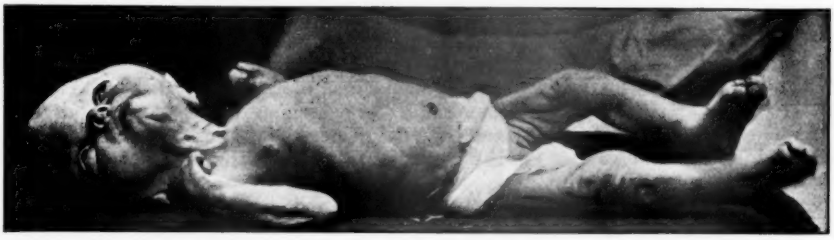

FIG. 1.—Acrocephaly with syndactyly. (Dr. Jean Smith's first case.)

and protruding. Face, characteristically diamond-shaped, widest at level of zygomatic arches. Palpebral fissures oblique, outer being considerably lower than inner. Eyes, owing to shallowness of orbits, protrude markedly; optic discs greyer than normal, and edges of right disc slightly blurred. Bridge of nose depressed; anterior nares look directly forward, and are unduly small. Palatal arch reduced to

a mere slit by encroachments of broad alveolar margins, along outer border of which is a shelf-like projection. Soft palate cleft; xiphisternum also bifid. Both hands and feet show syndactyly. First digit in both upper and lower limbs partially separate from rest of hand. Middle three digits are fused together throughout their

FIG. 2.

whole length and have one nail in common. Fifth digit separate from this main mass near the tip. Four outer toes joined together. Skiagrams of skull show digital markings and premature synostosis of sutures. Deformities of the metacarpals and phalanges are also seen. Mentality normal.

(II) Congenital Cranial Defect with Malformations of the Extremities.—R. F., male, 5 months. Skull and hands abnormal at birth. On examination, face is seen to be normally formed but anterior part of both parietal bones is flattened, rising to form well-marked ridge which projects to left of mid-line of vertex. Sagittal suture widely open along its whole length, beginning on forehead where it is half an inch wide and gradually expanding as it passes backwards over vault of skull until it merges into a large unossified area stretching across posterior and lateral aspects of vertex. Occipital bone seems well developed

but posterior parts of parietals are markedly deficient. Anterior part of right parietal bone shows a large depressed area. Eyes unequal in size, right smaller chan left; some degree of epicanthus present. Margins of external auricle are sharper and thinner than normal. Both hands are in a position of radial deviation and the small digit representing the thumb is freely movable in all directions. Feet normal. A systolic precordial murmur can be heard in all areas. Skiagrams show irregular ossification of frontal bone and diminished ossification of parietals. Both radii absent; first metacarpals very imperfectly formed.

Family History.—Mother, aged 40 and mother's sister have still two unossified areas in parietal bones close to mid-line. The only other child shows no abnormality.

We show these cases not from the point of view of diagnosis or treatment, but because associated deformities of the cranium and extremities are sufficiently rare

FIG. 3.—Congenital cranial defect with malformations of extremities. (Dr. Jean Smith's second case.)

to warrant their being brought before this Section and also because although the same title applies to both cases, they illustrate different aspects.

The first attempt to collect such cases was made in 1906 by Apert, who described nine examples. In 1920, however, Park and Powers were able to present records of no less than twenty-nine cases. They are of the opinion that although so few are reported, they are not so rare as the literature would lead us to expect.

The mental development in both the present cases is normal and in spite of the deformity these subjects of acrocephaly and syndactylism learn to walk at about the age of 18 months.

Discussion.—Dr. F. PARKES WEBER suggested that within the great class of congenital-developmental diseases of "mutational" origin it would be well to place all cases of associated congenital-developmental abnormality of the cranium and extremities into a

FIG. 4.

group which would include all varieties of acrocephalo-syndactyly, and would also include the second of the two cases now shown. The wonder was—not that there should be an unlimited number of varieties—but that such "mutational" cases, formed *de novo* from different families in various parts of the world, should fall into groups as well as they did. Evidently Nature, in producing mutations *de novo* from ordinary stock, tended to repeat certain simple or complex (i.e., associated) types, though often with considerable minor variations.[1]

FIG. 5.

Dr. E. A. COCKAYNE said that he disagreed with Dr. Parkes Weber. He considered that the first case was entirely different from the second. He had seen three or four children with acrocephalo-syndactyly, and asked whether this baby had an extra metacarpal bone, as was the case sometimes. Also, did the big joints move freely? In the last case which he had seen movement at the shoulders and elbows was limited by fibrous tissue, no proper joint having been formed. This was recorded of others also.

[1] For instance, there is a great difference between the case of acrocephalo-syndactyly shown by Dr. Norman Hill in 1929 (*Proc. Roy. Soc. Med.*, Clinical Section, 1929, xxii, p. 72) and that now shown by Dr. Jean Smith.

He believed there was one instance in which acrocephalo-syndactyly occurred in a parent and child; all other cases had occurred singly. He had never before seen anything like the condition in the second of these cases.

Dr. ERIC PRITCHARD said that with reference to a relationship between these cases and other cases of the same kind, it was curious that Jansen, of Holland, should have regarded them as all due to amniotic pressure occurring at different stages of fœtal life. Though this was a fanciful arrangement it was widely accepted, certainly on the Continent. Jansen classified anencephaly as the highest degree, with cyclops second, acrocephaly third, achondroplasia fourth, cleido-cranial dysostosis fifth, osteogenesis imperfecta sixth, and finally congenital dislocations of the hip. If the pressure occurred in the second or third week anencephaly resulted, and so on. It seemed more likely that they were due to a fault in the germ plasm.

He (the speaker) was much interested in the second case, in which there was a defect in the ossification of the parietal bones causing such extraordinary distortion of the external configuration of the skull. In the mother there was a similar condition: deep depressions and defective ossification of the parietals. It was reported that another relative had the same defect. In Hess's book on rickets and osteomalacia, recently published, the author described the frequency of defective ossification of small areas of the cranial bones, especially the parietal, mentioning that these defects were only revealed on close examination. He (Dr. Pritchard) was not familiar with defective ossification of this kind in cases of rickets, but Hess said that they were very common. Possibly such a condition as now shown could be mistaken for it.

Dr. JEAN SMITH (in reply) said there was some limitation of movement at the elbow, but no bony abnormality could be detected in the skiagram. So far as she was aware there was no other case of acrocephaly in the family, neither had the patient any extra metacarpal bones, but the second and third metacarpals gave the appearance of being fused, although that might be due to the position of the bones in the radiogram. In an exhaustive paper on this subject in the *American Journal of Children's Diseases* (1920, xx, 235) cases were recorded in which the patients had grown to adult life and their mentality had been normal.

Intussusception in an Infant.—JAMES CROOKS, F.R.C.S. (introduced by Mr. ERIC LLOYD).

Patient, female, aged 8 months. Admitted to the Hospital for Sick Children, July 27, 1930, with symptoms of intussusception of seven days' duration.

Operation.—Resection of 4 in. of gangrenous ileum, and side-to-side anastomosis. As the gangrene was limited to the small intestine, I was able to resect that part and anastomose small intestine to small intestine. I think that an infant is more likely to recover after such an anastomosis than after one involving the large intestine.

Eighteen days later, laparotomy was performed on account of acute obstruction due to plastic peritonitis, causing adhesions between two coils of small intestine above the anastomosis.

Result.—Complete recovery. (Patient shown and operations performed by kind permission of Mr. Tyrrell Gray.)

Milk Hypersensitivity with Eczema.—ROBERT COLLIS, M.D. (for DONALD PATERSON, M.D.).

G. C., female infant, aged 1 year and 10 months.

Breast-fed for two months; then put on a patent milk-food. At first attendance at the Hospital for Sick Children, Great Ormond Street, was having two feeds of cow's milk a day, custard, rusks and fruit; then aged 10 months; weight 17½ lb. *Previous History*: Continuous eczema since age of 4 months; occasional attacks of "asthma" and intestinal "upsets." *Family History*: Nil.

Was admitted to hospital in October, 1929, and put on half-cream. During six weeks in hospital patient vomited daily; had recurrent attacks of diarrhœa and lost 1½ lb.; eczema diminished under palliative measures.

December 18, 1929, attended out-patient department on account of another attack of eczema. Was skin tested and found to be markedly hypersensitive to lactalbumin, but not to casein. Was then 12 months old, weighed 16½ lb., had rickets, had no teeth, could not sit up and was covered with eczema.

On account of the lactalbumin hypersensitivity she was put on a balanced non-milk diet, vitamins A and D being supplied by radiostoleum, ♏ 5 once a day.

She gained ½ lb. in the first fortnight of this treatment, and 9 lb. in the succeeding nine months. The eczema diminished, the rickets disappeared rapidly, the teeth erupted and the child was soon able to stand and later to walk. She is now quite well and free from eczema and all other symptoms. She is still having non-milk diet and radiostoleum.

Note. Diet for G. C.—Take 4 oz. of liver or scraped meat, and having cut out tough portions of liver (make weight up to 4 oz.), heat in a double boiler for five minutes. Then pass through fine meat grinder and then through sieve. By these means it will be possible to produce a paste which may then be made into a solution with warm water. To this extract of liver or meat add: (1) Rolled oats or cereal 1½ oz., prepared by baking with water till fine jelly is made. (2) Sugar 3 oz. (3) Olive oil ½ oz. (4) Radiostoleum 4 drops. (5) Pinch of salt. Then add warm water to make up to 33 oz.

This served as a substitute for milk. Later it was possible to add more solid constituents as the teeth appeared. Four feeds of 8 oz. each were given a day. One teaspoonful of orange juice was also given.

POSTSCRIPT.—A few days ago a typical attack of asthma developed with eosinophilia and a marked hypochlorhydria.

Dr. G. W. BRAY said he had watched this case for some time, and thought it possible that the eczema was undergoing spontaneous cure. The change in diet had not affected the onset of asthma. The child showed skin reactions to lactalbumin, not to casein. Lactalbumin was coagulable by heat, and rapidly lost its sensitizing properties when the milk was boiled. With the hypochlorhydria in the case, an acidified boiled milk would have brought about a similar amelioration of the condition without the trouble or expense of the liver preparation. As to the skin reactions during infancy, most infants showed reactions to foods, but as they became older reaction to inhalations predominated. When this patient first came to hospital some months previously, the lactalbumin reaction was definitely positive, but it was now diminishing and the reaction to feathers was at the present time positive.

Cerebellar Cyst: Result after Operation.—CARLYLE T. POTTER, M.D. (for Dr. DONALD PATERSON).

A. B., girl, aged 8½ years, attended the Hospital for Sick Children, Great Ormond Street, in June, 1930, complaining of headache and vomiting, and difficulty in walking.

Previous History.—Pertussis at 3½ years, followed by internal strabismus which is still present, measles at 5½, mumps and chicken-pox at 6, scarlet fever at 7, diphtheria in November, 1929.

Family History.—One brother, aged 5 years, healthy; father died from pulmonary tuberculosis five years ago.

History of Present Condition.—Except for infectious diseases, patient had good health until she contracted diphtheria in November, 1929. Soon after this she began to have attacks of generalized headache and vomiting, occurring at intervals of from three to four weeks. After the attack she experienced giddiness. Walking became unsteady. Headache and vomiting increased in severity, walking

was more difficult and the left arm became unsteady in movements. The child let things drop, spilled her milk, and could not carry out fine movements with her left hand. Her mentality gradually became dulled.

Physical examination showed weakness of right and left external recti; bi-lateral papilloedema of about 3 D.; lateral nystagmus; inco-ordination of left arm and leg; tendon jerks greater on right side than left, and a right extensor plantar response. Patient walked unsteadily on a wide base, with tendency to incline to left, holding out right arm to balance herself. Three days later her mental condition was such that she did not recognize anyone. The blood Wassermann reaction was negative.

Operation.—Mr. Barrington-Ward carried out a two-stage operation. When the dura was exposed the left cerebellar lobe was tense and bulging, and pushing the right lobe across. When the dura was incised the left lobe immediately herniated. The left lobe was punctured and clear yellow fluid escaped. Opening enlarged and found to lead to a smooth-walled cyst with thin cerebellar tissue over it. On emptying the cyst the cerebellum collapsed. There was no evidence of neoplasm.

Examination of fluid: Blood-stained, serous, straw-coloured, high protein content. No cells and no organisms seen. Leishman-stained films showed many red blood-corpuscles and a few leucocytes. No abnormal cells. Culture sterile.

Section of wall showed small portion of normal cerebellar tissue and one small portion of more cellular structure consisting of three or four layers of flattened endothelial cells with connective tissue between. The appearance was that of a simple cyst of the cerebellum showing a small portion of its lining endothelial layer.

Since the operation the patient has made steady progress. There has been no headache or vomiting, and her mentality has greatly improved. There is no nystagmus. The fundi show only slight swelling of discs with no hæmorrhages. There is slight irregular pallor of discs, but vision is excellent. There is still some ataxia of the left arm and leg but walking and use of the left arm have greatly improved.

Hæmolytic Jaundice.—W. M. FELDMAN, M.D.

Joan R., aged 7 years.

Past History.—Born in Australia. Pallor and languor since infancy. Measles, whooping-cough.

Family History.—Mother, pulmonary tuberculosis. Sister, tuberculous adenitis. Otherwise negative.

In-patient St. Mary's Hospital, Plaistow, April 11, 1927 (when aged $3\frac{3}{4}$ years), on account of anæmia, with splenic enlargement (spleen two fingers' breadth below costal margin), subacute otitis media (right ear), and irregular mild pyrexia. Widal and Wassermann reactions negative.

Blood then showed: R.Cs., 3,560,000; Hb., 80%; C.I., 1·1; W.Cs., 7,800; *Differential count:* polys., 40%; lymphos., 57% small; lymphos., 1% large; eosinos., 1%; monos., 1%.

Discharged July 10, 1927, spleen just palpable. Improved general condition.

Re-admitted September 15, 1930, with pallor, spleen four fingers' breadth below costal-margin, mild intermittent abdominal pain and mild pyrexia.

Blood, September 16, 1930: R.Cs., 3,664,000; Hb., 60%; C.I., 0·8; W.Cs., 7,600; *Differential:* polys., 53%; lymphos., 45%; eosinos., 2%; Wassermann reaction, negative. *Fragility* of red cells increased, there being a trace of hæmolysis in 0·65% saline. Further blood examinations showed little change.

I ask for opinions as to diagnosis. As there is a history of jaundice in the child a few months ago and also in a maternal uncle, for a short time, this is almost

certainly a case of congenital hæmolytic jaundice. The question therefore is whether splenectomy should be performed, or whether I ought to wait until more urgent symptoms arise.

[In the discussion on this case it was generally agreed that splenectomy was advisable, in view of the probability of serious crises, and of the marked improvement in general health which usually followed such operations.]

? Endothelioma of Foot.—ERIC I. LLOYD, F.R.C.S.

Patient, boy, aged 8 months.

At birth a small nævus was present between the second and third toes of the left foot.

On September 29, 1930, this was cauterized, as it was increasing in size. Since then there has been a rapid increase in size, and it is now a tumour pushing the toes apart.

X-ray examination, negative.

The tumour is a neoplasm of some degree of malignancy. I propose to excise it under a tourniquet and, if necessary, I shall afterwards apply radium.

Section of Obstetrics and Gynæcology.

President—Sir EWEN MACLEAN, M.D.

[*October* 17, 1930.]

Vaginal Metastases in Carcinoma of the Body of the Uterus.

By GILBERT I. STRACHAN, M.D., F.R.C.S.

THE occurrence of metastatic nodules in the vagina in cases of carcinoma of the body of the uterus not only constitutes an interesting pathological problem but is at the same time an important clinical factor, as it represents a prognostic feature of grave omen in what might otherwise be a favourable case.

In a series of thirty cases of carcinoma of the body of the uterus, I have found these metastases in five (16·7 %), and a sixth case is also included in this series by permission of Sir Ewen Maclean, whose patient she was.

Case I.—Nullipara, aged 39, sent to me in August, 1927, a diagnostic curettage having been performed two weeks previously, and adeno-carcinoma diagnosed by the microscope. The uterus was bulky, but mobile, and on the lower part of the left vaginal wall was a secondary nodule about three-quarters of an inch in diameter. The vagina above was quite normal, with no induration. Total hysterectomy was performed and the vaginal lesion removed by wide local excision. The microscope showed adeno-carcinoma in both areas. The pelvic condition remained clear, but vaginal recurrence took place, for which radium was applied. Later the left inguinal glands became involved and the patient finally died, sixteen months after operation.

Case II.—Multipara, aged 64, came under my care just recently. She had a fibroid half-way up to the umbilicus, with carcinoma of the body and some posterior anchoring of the uterus, which contra-indicated total removal. The cervix was patulous and a secondary submucous nodule was present one inch below the cervix on the right lateral vaginal wall, with an area of apparently healthy mucosa intervening. Radium was applied to the interior of the uterus and buried in the vaginal growth, but it is too early yet to judge the result. In this case again, the microscope showed adeno-carcinoma both in the uterus and in the vaginal nodule.

Case III.—A multipara, aged 65, seen in June, 1926, with early carcinoma of the body, the uterus being only slightly enlarged and freely mobile. Hysterectomy was performed and radium applied later to the vaginal vault. The immediate result was good, but six months later a nodular secondary growth was found on the lower part of the anterior vaginal wall, just above and to the right of the urethral orifice. The rest of the vagina, including the vault, was quite free of any recurrence. There was no sign of this either at operation or when the patient was last examined, six weeks previously. The application of radium controlled the growth to a certain extent, but the patient died, ten months after operation and four months after the first appearance of the vaginal nodule.

Case IV.—A nullipara, aged 52. Sir Ewen Maclean performed total hysterectomy for carcinoma of the body in February, 1927. Five months later the patient presented herself with blood-stained vaginal discharge. The vault of the vagina was securely healed and clear, but a small, hard, secondary nodule, the size of a hazel nut, was found about the middle of the posterior vaginal wall. This was excised, and 100 mgm. of radium inserted into the wound for twenty-four hours. Microscopic examination showed a very glandular type of adeno-carcinoma. Healing was immediate, and now, three years and three months afterwards, the patient is going about her duties entirely free from symptoms.

Case V.—This presented certain uncommon features. The patient was a multipara, aged 53. I saw her in March, 1930, and the history was that the uterus had been removed for cancer nine years previously, and that she had had blood-stained vaginal discharge for the last year. Local examination demonstrated a large exuberant growth springing from the right vaginal wall. Under anæsthesia it was easily detached, and the area of attachment

showed no induration. The stump of the cervix was present but was unaffected and freely mobile. Microscopic examination showed proliferating adeno-carcinoma. Radium was applied, in a bullet, to the area of attachment, and up to the present there have been no signs of recurrence.

Case VI.—A multipara, aged 56, sent to me in April, 1929, with what appeared to be a primary ulcerative nodular epithelioma of the vagina in the lower part and anteriorly. The cervix and uterus were free and normal for her age. Radium was applied and a section taken showed, to our surprise, adeno-carcinoma. Immediate curettage of the uterus removed only a small amount of atrophic mucosa, which showed no signs of carcinoma. Local improvement was rapid, and when seen seven months later, the vaginal condition had clinically healed, while the uterus remained normal on examination. One month later, however, the uterus was found enlarged by two inches and hard, with the cervix patulous. The curette now removed typical carcinomatous material, and laparotomy showed secondary deposits on the anterior abdominal wall, while the omentum was occupied by a large carcinomatous cake. Under these circumstances hysterectomy was abandoned. She has since died, thirteen months after the first examination and five months after the uterine condition declared itself.

It will be noted that these cases fall into three categories. In the first are the two cases in which vaginal metastases were present before operation and when the patients were first seen. In one of these curettage had been performed two weeks previously.

In the second are three cases in which metastases were discovered for the first time at varying intervals after hysterectomy. The intervals were six months, five months, and nine years. In the last case, while the original condition of "cancer of the womb" could not be verified, the presence of the adeno-carcinomatous nodule lent support to the history. In the third category is the single case in which adeno-carcinoma was found first in the vagina and only eight months later in the uterus with very rapid development and spread. In none of these cases was there any submucous vaginal infiltration extending downwards from the uterus, as is so often seen with vaginal extension of carcinoma of the cervix.

Three main methods of such metastatic formation spring to mind: by direct implantation, by lymphatic extension, or by blood-stream transference. The theory of direct implantation is not favoured by most observers, although in some cases it would appear the most simple explanation. The points in its favour are the fact that the deposits are usually in the middle or lower vagina with healthy mucosa above. Again, in most of these cases the patients are multipara having more or less patulous cervices, so that expulsion of a few cancer cells would be easily understandable. The possibility of exploratory curettage causing cellular implantation in this way has, however, to be taken into account, while the manipulation of the uterus during hysterectomy would tend to such cellular detachment and extension if the cervix were not previously sutured. It has to be remembered also that any area of vaginal trauma would act as a suitable nidus for the growth of such implants, but this consideration does not appear to arise in the cases reported here.

In this connection, however, Schopf, in 1891, reported the development of carcinomatous nodules in the vaginal scar, three months after vaginal hysterectomy, while Hofmeier, in 1895, reported a similar complication less than a year after the same operation. Similarly perineal wound implantation in a Schuchard's incision has been reported by Hirsch, Milner and others. Cullen does not favour the theory of direct implantation, as he considers that any cells cast off from the interior of the uterus in this condition are likely to be necrotic and, therefore, unable to survive in new surroundings. This, however, is not necessarily the case and, especially in the polypoid type of uterine carcinoma, it would be easy to visualize the detachment of a small group of living cells which could gain vaginal implantation with subsequent growth.

Retrograde lymphatic extension is the explanation accepted by Cullen and others, although Ries, in 1918, reported a case in which vaginal metastases occurred eighteen

months after hysterectomy for corporeal carcinoma. He excised the vagina, and in five hundred serial sections could find no trace of lymphatic involvement. Retrograde lymphatic extension is regarded as the usual mode of progress of carcinoma of the cervix, as has been shown by Leitch, who found more or less extensive vaginal involvement in 97·5% of cervical carcinomas investigated by him post mortem. But in these cases the condition is usually a submucous induration continuous with the parent cervical growth, and has no resemblance to the isolated nodules under discussion. It would appear that retrograde lymphatic extension has been assumed or taken for granted rather than proved as the mechanism of this extension, as the literature shows no actual evidence on which definite acceptance can be based.

Transmission by the venous blood-stream, as in the case of chorio-epithelioma, is not usually regarded as a causative in this connection. It is well known that blood-borne metastases are not common in corporeal carcinoma, although such cases are reported from time to time. Again, vascular tissue does not appear to exert the same attraction for adeno-carcinoma that it does for chorio-epitheliomatous tissue, and if such vascular transference of growth should ever occur in these cases, it must be in a small proportion.

The case most difficult to explain in the series is the last, in which the uterine carcinoma became evident, although previously looked for, only eight months after the vaginal growth. Cullen has reported a similar case, in which, however, the uterine condition developed one year after the vaginal nodule and was also inoperable.

The matter of vaginal metastases in uterine carcinoma has been discussed by several other observers.

Wilson had one such case in his series of 38, while J. V. Meigs, of Boston, found the condition present in 12·1% of 206 case histories investigated by him.

It is of interest to note that Ewing in his "Textbook of Neoplastic Diseases" makes no mention of this complication of uterine carcinoma, while Wilfred Shaw, who was good enough to look up this subject for me in Halban and Seitz's large German "System of Gynæcology," tells me that the matter is not discussed there.

While the pathological problems raised are of interest and importance, the clinical aspects of the matter are equally important. Obviously this complication adversely affects the prognosis. In three of the six cases reported here the patients are dead, and although of the three living, two are free from symptoms, the period of clinical cure is too short for a final result to be judged; the third case has come under treatment too recently for the outlook to be judged.

From the fact that the vaginal condition was seen before operation in three out of the six cases reported, it may be deduced on the one hand that, if the extension is by lymphatic permeation, pre-operative suture of the cervix is useless, while, on the other hand, if the theory of direct implantation is accepted, cervical suture should always be performed and accompanied by thorough but gentle vaginal cleansing previous to hysterectomy. It has been said that such vaginal nodules are unusually susceptible to radium, but as the reaction has been satisfactory in only two out of our six cases, with a third case *sub judice*, we cannot share this impression, although the available material is limited for the purpose of reaching a general conclusion.

In the presence of such a metastatic deposit with an early carcinoma of the body, it has to be considered whether hysterectomy is justified, followed by radiation or excision of the vaginal nodule, or even by removal of the vagina, and in this respect our personal inclination would be rather in the negative direction.

Finally, the necessity for carrying out a careful examination of the vaginal mucosa in all cases of corporeal carcinoma is demonstrated.

I am much indebted to Sir Ewen Maclean for allowing me to include his case in this series.

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Discussion.—Sir EWEN MACLEAN (President) said he would add to Dr. Strachan's series a further case in which the patient, aged 68, 1-para, when first seen by him, gave a history of blood-stained vaginal discharge for four months and practically no other symptom. Hysterectomy was not permitted, although the exploratory curettage revealed typical adenocarcinoma of the body of the uterus. Forty-five millicuries of radon were inserted into the cavity for twenty-four hours. One month later nodules were found in the lower part of the vagina and these, on microscopical examination, were found to reproduce the histology of the uterine scrapings.

Three months after the original investigation, subcuticular nodules appeared in the calf of the left leg, the anterior margin of the left axilla and the left suprasacral region. These also had the same histological appearance as the vaginal nodules and uterine scrapings; the vaginal and skin nodules having additionally, of course, the dermal tissues.

During the following month a persistent dry cough developed, with the signs and symptoms of mediastinal growth and the patient died some weeks later. The case clearly illustrated blood-borne metastases.

Dr. J. S. FAIRBAIRN said that he would be prepared to accept all the three routes of dissemination mentioned as possible. The case described by the President was a good instance of blood-stream diffusion and the lymphatic path was so general in carcinoma that its possibility could scarcely be denied in these cases. Direct implantation in the vagina seemed the least likely, for the uninjured vaginal skin would appear an unfavourable nidus, but he would mention a case of his own that seemed to be an example of it and differed from those quoted in the paper by having no discrete nodule but a wide diffusion over the vagina. The patient was a nullipara, aged over 60, who had had post-menopausal bleeding, and on whom he had performed hysterectomy. She had twice been curetted by her general practitioner, the first time eight months previously, and the second time a fortnight before operation. The report on the first scrapings was that they were not malignant, but the report on the second was that they showed adenocarcinoma. Some roughness of the vaginal wall was noticed at the second curetting, and examination before operation gave the feeling of a sandpaper-like surface to the vagina. The condition was thought to be either a senile granular vaginitis or a diffuse carcinomatosis. The uterus contained a large fundal growth, with smaller nodules in the lower part and in the cervical canal.

Later, the vagina became covered with a soft growth, reported on as an adenocarcinoma, which was treated on several occasions with radium. The patient survived for six years after the original hysterectomy.

Dr. Strachan's paper raised the important practical point of the danger of the diagnostic curettage. The question would be decided only when we had sufficient information of the relative risks of the performance of hysterectomy in all cases of possible cancer of the uterine body and of increasing the danger of spread of cancer. The great majority of such diagnostic curettings he had performed had been negative, but it would be advisable to avoid the procedure in all cases in which the diagnosis was strongly in favour of cancer. Without the use of the microscope there would, however, be many errors.

Mr. DONALD ROY said that he had had three unusual cases of this condition probably illustrating three methods of spread. The first a case of early operable carcinoma of the body was treated by abdominal panhysterectomy without preliminary curettage. Many small superficial nodules of growth were noted at the vaginal orifice when the patient was first seen, and were treated by applying 75 mgm. radium element in three flat containers with a screenage of 3 mm. of lead for 24 hours, at the same time as the hysterectomy was performed. The patient made a complete recovery so far as the pelvic condition was concerned and was free from pelvic growth six months later when a metastasis developed in the left tibia and she was lost sight of. This case appeared to illustrate dissemination by implantation and by the blood-stream.

In the other two cases the patients were obese women with advanced carcinoma of the cervix. The condition was considered to be inoperable for local and general reasons. In one

of these cases there was in addition a large fibroid of the uterus. Both the cases were treated with radium by a somewhat modified Heymann technique, some needles being inserted into the growth as well. No vaginal metastases were present at the time. In both cases six months later, metastases developed in the lower third of the vagina and vulva in almost identical positions deep to the vaginal skin. There were no metastases within the sphere of action of the radium and clinically the cervix and parametrium remained free from recurrence.

The nodules were anteriorly on both sides of and below the urethral orifice and along the lower third of the posterior vaginal wall near the midline. In one case there was also a nodule in the ischio-rectal fossa. The nodules disappeared completely under moderate radium dosage by needles deep to the nodules and superficial application to the vaginal surface. At the same time, inguinal gland enlargement was noted and the glands were excised and found to contain degenerating carcinoma. Now, eighteen months later, one patient had a nodule between the coccyx and the rectum. The other was at present free from obvious recurrence. Both had retained their general health and had followed their employment between admissions to hospital, so that persistent treatment of this kind had been worth while. There would appear to be important lymph channels passing down to the neighbourhood of the urethral orifice, which was an unhappy position for metastases to remain untreated.

The Organization and Methods of Practice of the East End Maternity Hospital.

By W. H. F. Oxley, L.R.C.P., M.R.C.S.

The East End Maternity Hospital has been frequently referred to during the last few years as an institution which has attained a high degree of success, and it may therefore be of interest to give a brief description of its work. In doing so stress will be laid upon those points where its practice differs from that generally accepted, and where judgment as to the relative value of clinical methods not in accordance with modern teaching appears to have contributed to good results.

The hospital was established in 1884, and up to the end of 1929 had attended 51,487 cases of childbirth, with a maternal death-rate throughout that period of 1·35 per thousand, and since the year 1921, of only 0·68. Although clinical notes have been taken through the whole of its existence it is only since 1925 that these have been carefully compiled, and it is upon these, which comprise 10,376 cases, that this paper is based. It is felt that this number of cases is large enough to enable some reliable conclusions to be drawn, both as to the incidence of complications in an unselected sample of the child-bearing population of the East End of London, and as to the value of the organization and methods of practice of the hospital.

The building.—As the hospital has grown from a small beginning, the building is by no means in accordance with modern ideas of hospital construction, the stairs being many, the passages narrow and the wards small. Although these conditions make the work heavy, they are not altogether a disadvantage, for they help greatly in the isolation of patients, staff and utensils, and make frequent "spring cleaning" more feasible, and so are important factors in keeping down the sepsis rate. The hospital now contains fifty-six beds arranged in wards of from three to eight beds.

The staff.—The hospital is under the direct management of the Lady Superintendent, a fully trained and highly skilled nurse and midwife, whose genius for organization and management is largely responsible for the successful work. She has a staff of six midwives for the hospital and two for the district. There are about thirty pupil midwives, who do the nursing as part of their training. There is no resident medical officer, the medical staff consisting of general practitioners in the neighbourhood, normally three in number, appointed by the committee of management, who have always followed the advice of the senior medical officer in this matter. Control of the medical work is vested in the senior medical officer, also a general practitioner. He is called in for every abnormality, pays a routine

visit every morning, delivers midwifery lectures and holds one ward clinic, one ante-natal session and one post-natal session weekly. The assistant medical officers relieve the senior as required. There have been only two senior medical officers during the forty years of the hospital's existence, so that continuity of methods over a long period of time has been attained. Some of the advantages of this method of staffing are that the medical officers gain experience, the value of which must be reflected in their general practice; they have no hesitation in sending into hospital their difficult cases, while the absence of a junior resident staff diminishes the likelihood of premature interference with the normal course of labour. There is a good staff of consultants, one of whom is always at the service of the medical staff as required.

The patients.—About 2,000 women are attended annually. They are almost exclusively resident in the Metropolitan Boroughs of Stepney and Poplar; rather more than one-half are admitted to hospital, the remainder being attended in their own homes. The majority of the primigravidæ and all cases in which abnormal labour is anticipated are booked for admission into hospital and abnormal cases booked for attendance on the district are admitted at the discretion of the medical officer.

The patients are unselected. Any married woman applying for attendance is accepted unless she is found upon inquiry to be able to afford reasonably suitable facilities for herself; no patient has ever been refused upon medical grounds. There are, however, many doctors and midwives who send cases which they consider are likely to prove abnormal; these are booked and attended and their records are included in this analysis, thus slightly raising the abnormality ratio.

On account of the danger of admitting potentially infected cases, as few emergencies as possible from outside sources are treated. It is impossible to exclude them altogether; they numbered about ten during the five years under consideration and were mostly cases of toxæmia and hæmorrhage. No cases of failed forceps were admitted during this period. A few unbooked cases were also admitted on account of sudden onset of labour in the street.

Every abnormal condition arising in its patients, whether during pregnancy or labour, has been treated by the hospital, but the following nine cases were removed elsewhere during or after the puerperium:—

Four cases of puerperal mania were removed to the infirmary.

A case of white leg, in which the temperature had been normal for some time but the swelling still remained, was removed to the infirmary at the end of six weeks.

A woman with an ovarian cyst was removed to a general hospital for operation at the end of a normal puerperium.

A woman with a very large pyonephrosis of old standing was removed to hospital at the end of the puerperium for operation.

These patients all recovered.

A woman with a very large stone in the kidney was removed to hospital, at the end of the puerperium. At operation the whole kidney substance was found destroyed and she died two hours after operation. Her death has not been included in the hospital returns as it had nothing to do with her child-birth.

A woman with pelvic cellulitis following a difficult forceps delivery was removed to a general hospital, where she died. Her death is included in the hospital returns.

These are the only patients who were discharged otherwise than in good health and the inclusion in the returns of the one case of death from puerperal causes keeps the records correct.

The Work of the Hospital.

Ante-Natal Department (Table I).—This work follows the usual lines, except that all the routine work is done by a midwife and only those cases which she picks out as abnormal, or potentially abnormal, are seen by the doctor. It is found that in

this way the midwives are trained to have a sense of responsibility and that their interest in the work is enhanced, while the results show that the system has been effective. It must be admitted, however, that skill above that of the average midwife is required.

The attendance of every woman is compulsory and is easily secured; there is an efficient following-up scheme which is seldom required. Booking takes place about the sixth month and from the seventh month all primigravidæ attend fortnightly, the multiparæ three times. This is as far as opinion in the neighbourhood will go at present, and as the results have been good, no attempt has been made to bring the number of attendances up to a standard which could probably not be enforced.

The pupils are taught to diagnose presentation and position in every case and to make a forecast of the probable course of labour. Special importance is paid to this, and some of the pupils get quite expert at it.

The discovery of albuminuria is left to the midwife, who is instructed to bring every case, however slight, before the doctor at once. In some of the milder cases, home treatment is given for a week, followed by admission if it has not then cleared up, but all serious cases are admitted straight away. The usual drastic eliminative treatment is given but, if anything, more drastically. That this method of selection by the midwife, combined with immediate treatment, is effective, is shown by the almost entire absence of eclampsia. In these 10,376 cases there were no deaths from eclampsia and only two slight cases, each having one fit after delivery and making a good recovery.

Purulent vaginitis and cervicitis are treated by thorough swabbing of the cervical canal with picric acid in spirit, and in some cases the canal is scraped with a Volkmann's spoon. One treatment, followed by simple douching for a week, is usually sufficient. There appears to be no danger of bringing on premature labour.

A Wassermann test is carried out on all patients with a suspicious history, but in only eight cases in this series was the reaction positive; the patients were all treated at a general hospital, returned for their confinement, and had healthy full-time babies.

Valvular disease of the heart was a frequent occurrence. In nearly all the cases compensation was good, and the cards were marked for special care during labour. A few were admitted for antenatal treatment; in six cases induction was performed, and in some the second stage was deliberately shortened by the use of forceps.

Dental caries is common and treatment is arranged for, but the patients are loth to submit to it, under the mistaken idea that it will bring about miscarriage. There is no clinical evidence that this or indeed any other "septic focus" has been a cause of sepsis.

Other general diseases requiring treatment were anæmia, two of which were pernicious in type, otitis media, epilepsy, bronchitis, etc.

Antenatal Beds.—Three beds are set aside for antenatal cases, and proved ample for the needs of these 2,000 cases per annum.

Deliveries.

Table II gives a summary of the deliveries. It will be seen that nearly all the primiparæ were admitted to hospital. This was in order to ease the work and not for any medical reason. In fact, they get on just as well, if not better, in their own homes. (See Table XI.)

Occipito-posterior positions (Table III) occurred in 12% of the vertex presentations in the hospital. Although they are not usually classed as abnormalities, yet in many cases they give the greatest anxiety to the attendant. They form the commonest indication for the use of forceps, no less than 11% having to be thus terminated, even with the conservative midwifery practised by the hospital. The long first stage causes exhaustion of the mother, and the temptation to interfere

prematurely can only be combated by the exercise of great self-control, and they do in fact comprise a large number of the "failed forceps" cases reported in the journals from time to time.

On account of these difficulties, attempts are made to rotate them antenatally by means of Buist's binder. It is not easy, however, to be dogmatic as to its effect, as in a large number of presentations correctly diagnosed as posterior before engagement, the head enters the pelvis anteriorly. It certainly has no effect when the head is engaged, but one is inclined to think that if the head is late in engaging, either through deficient flexion or disproportion, it does influence rotation. We have certainly had fewer very prolonged cases since it has been used systematically.

With regard to treatment, these cases remain the most difficult with which we have to deal. Rotation before full dilatation, air-bags, etc., have been tried and given up and reliance has to be placed upon securing rest and comfort for the mother during the first stage, by means of humanity and attention, together with the aid of morphia. Rotation by forceps is not employed.

Breech presentations. (Table IV.)—During pregnancy the child presented by the breech in 535 cases. Although cephalic version has been practised for many years and some degree of skill attained, it has been found impossible in many cases. Extension of the legs, posterior positions, twins, and the leaving of the attempt until after the thirty-second week, especially in primiparæ, are common causes of failure. The result is that considerably more than half eventually come into labour as breech. These include all the unsuccessful cases, those not diagnosed and a number in which an easy delivery was anticipated and which were, therefore, left for teaching purposes.

316 cases came into labour as breech; spontaneous delivery took place in 256, manual extraction was necessary in fifty-five, and forceps were applied to the after-coming head in five. Forceps were not applied to the breech nor was the use of the blunt hook required.

The result to the child is the criterion of success or failure in breech delivery (Table V). This has been emphasized by Gibberd [1], who compiled the returns of the breech presentations of six maternity hospitals and found that 30% of fœtuses were stillborn, and 9% died before the fourteenth day. Upon these results he made a strong plea for turning in every case; he admitted, however, that there were some failures. Eardley Holland [2] reported that 75% of stillbirths and neonatal deaths were due to cranial stress during too rapid delivery, and expressed the opinion that these could be largely reduced by careful delivery. In this series the stillbirths were 12% and the neonatal deaths 5%. These, although only half the numbers given by Gibberd, are still high figures and appear to confirm his contention, but if the analysis in Table V is referred to it will be seen that birth trauma and asphyxia have practically disappeared, the outstanding causes of death being prematurity and death of the fœtus before labour. In only ten stillbirths and four neonatal deaths—that is, in 4·4%—was breech presentation possibly responsible; in most of the others the death or prematurity of the fœtus was probably the cause of the breech presentation.

If, therefore, it is possible to reduce the danger of breech presentation to the child to such small dimensions, it would seem doubtful whether it would not be wiser, in teaching schools at any rate, to leave all cases unturned, in order that the pupils may be thoroughly trained to deal with those cases which they will undoubtedly meet with in practice.

The advantage of the combination of experienced doctor and midwife is better seen in the management of breech cases than in any other branch of midwifery. The practice followed in the hospital is that the midwife makes fairly frequent examinations in cases likely to be difficult, and is so able to call the doctor just before full dilatation and before impaction has taken place, so avoiding the temptation of premature extraction.

Before commencing manual extraction the forceps are boiled and placed at hand for immediate use, and a hot bath is prepared to resuscitate the child. Care is taken in all cases thoroughly to stretch and smooth the vagina by hand, a process taking several minutes, and to use great gentleness in extraction, any necessary traction being made strictly in the axis of the pelvis and assisted by fundal pressure. The value of the good midwife who knows how to give the final suprapubic pressure in the right direction just as the head is coming through is enormous, and contributes greatly to the results. It is found that great haste in delivery is not necessary, the fœtus being able to withstand occlusion of the cord for well over five minutes, provided violent attempts at resuscitation are not made, so that if one knows what to do there is ample time to do it.

It is, therefore, considered that all pupils, midwives as well as medical students, should be well drilled in the management of breech emergencies, rather than that an attempt, which cannot be wholly successful, to side-track them altogether by turning, should be persisted in.

Obstetric Operations.

(Table VI.)—Induction was performed on 126 occasions (1·2%), 63 of which were for contracted pelvis and 48 for toxæmia. Two mothers died, but, as will be seen later, their death was probably not attributable to the induction; in the others the puerperium was normal. Fourteen infants were born dead.

Unless the case is urgent, intensive induction by hot baths, douches and enemata, together with three doses of quinine, ten grains, by mouth, is tried. Where this is unsuccessful and in cases of urgency, Krause's method is adopted. This is carried out in the usual way, except that an anæsthetic is given only when the patient is very nervous. If carefully performed, the operation is entirely painless, and it is thought that the psychic effect helps in its success.

If an anæsthetic is needed in cases of toxæmia, "A.C.E." is used and stopped as soon as the patient is under, the operation being easily completed before she comes round.

Induction is usually performed for cases of albuminuria if they do not clear up after 14 days' treatment, not so much for fear of eclampsia but because it is thought that prolonged albuminuria leads to permanent kidney trouble and very likely to death of the fœtus.

Forceps were applied on 302 occasions, a percentage of 2·9; due consideration was given in each case, and they were never used without a definite indication. They were never applied to a head above a brim. It will be seen that persistent occipito-posterior positions account for more cases than contracted pelvis, and form, in fact, the commonest indication for their use.

Two mothers died (see later) and four others had a slightly morbid puerperium. The morbidity in these cases, all of which were abnormal, was thus 1·6%, as compared with 1·1% for the whole series, and it would therefore appear that the proper use of forceps is not followed by greater risk of sepsis than is spontaneous labour.

Cæsarean section was performed on one occasion only. This was a case of generally contracted pelvis in which induction had been done in a previous labour, with a stillborn child.

Craniotomy: No cases required this operation.

Podalic version was performed during labour 35 times, 27 of which were for antepartum hæmorrhage, while transverse presentation, prolapse of the cord and flat pelvis accounted for the remainder.

Manual removal of the placenta was necessary in 73 cases. In two of these the patients died from sepsis, and, although they had other complications, this was probably the predominant cause; in one case, otherwise normal, peritonitis

developed, the patient recovering after laparotomy; in four there was a rise of temperature clinically diagnosed as due to septic absorption. This gives the incidence of sepsis as 10% and establishes the procedure as the most dangerous operation in the realm of midwifery.

The smallness of the number of cases of contracted pelvis of sufficient degree as to necessitate interference with the course of labour is remarkable.

They were as follows: induction, 63; forceps, 64; version, 1; Cæsarean section, 1; total, 129 (1·2%).

Several cases sent by doctors with a view to Cæsarean section did not need it and on some occasions women who had previously had the operation performed were delivered of a full-time healthy child without it.

Although the policy of non-interference has been here carried to the limit consistent with safety, it is only fair to state that other hospitals working on entirely different lines obtain very good results. One of these, situated in London and dealing with the same class of cases as the East End Maternity Hospital, is compared with it in Table VII. From this it is seen that the total interference, apart from the third stage of labour, in the hospital referred to is nine times as great as in the East End Maternity Hospital, inductions being nineteen times, forceps four times and Cæsarean sections one hundred and ninety times as many. As these two hospitals obtain results of the same order of merit, it would appear that it is not so much the method or details of treatment which counts, as the spirit which actuates the whole of the work. It is difficult to imagine, however, that interference for real or suspected difficulty, to the extent of one out of every three cases of labour, can be necessary, or that good results can be obtained thereby save under the best hospital conditions.

It would almost seem that some obstetric surgeons still make a mere diagnosis of contracted pelvis a reason for performing induction or Cæsarean section, irrespective of the relation of head to pelvis and other considerations, whereas in the hospital at least 80% deliver themselves spontaneously and the remainder have been treated with the results shown, either by forceps or by induction, at about the thirty-sixth week.

That the number of deaths following Cæsarean section is by no means negligible is seen by reference to the Report of the Departmental Committee on Maternal Mortality, which found them to amount to 112 out of 2,000 deaths investigated, and considered that many of these deaths could have been avoided had proper antenatal care and foresight during labour been available. In other words, the skill of the obstetrician in ante-natal diagnosis is in inverse proportion to the number of his Cæsarean sections and, I would like to add, to his forceps cases as well. Although the proportion of one section to 10,000 cases can hardly be expected throughout the country, since contracted pelvis of a severe degree is uncommon in London, it seems as if a large number of unnecessary operations were being performed.

Antepartum Hæmorrhage.

(Table VII, A.)—Ante-partum hæmorrhage occurred in 119 booked cases and four emergency cases were admitted. 74 were accidental and 49 placenta prævia. Only 23 occurred in primigravidæ and a striking feature was that many of the severe cases were found in elderly multiparæ.

Accidental hæmorrhage: Those cases in which, after delivery, a retroplacental clot was found without the condition of mother or child having been affected are not included.

In eighteen cases hæmorrhage was altogether concealed and gave rise to signs and symptoms, but only three of these were of the severe type with collapse of mother and tense, tender uterus, two of them being emergency cases in which there had not been any antenatal examination. It would therefore, seem that antenatal

care, by reducing toxæmia, does reduce the incidence of these severe cases and this probability is confirmed by the result of urine examination, as albumin was present in only two cases to any great amount, ten others having a mere trace. The treatment in most cases was the usual tight binder and rupture of membranes.

No patient in the booked cases died and all but one had a normal puerperium. Of the two emergency patients who died, one was collapsed when first seen and the other had a misleading concealed hæmorrhage at 24 weeks' gestation.

Placenta prævia: Of the 49 cases of this condition, 12 were primigravidæ and 27 were premature. Nine were central.

Each case was treated on its merits; premature cases with good pains required no special treatment, except sometimes an injection of pituitrin; for those at or near term the classical treatment of "early turning, slow extraction" was adopted in most cases, slow extraction being interpreted to mean spontaneous expulsion by the uterus, sometimes with the help of a 2-lb.weight. All mothers recovered, but three had slightly morbid puerperia.

Results.—Here is a consecutive series of 119 booked cases of antepartum hæmorrhage without a maternal death.

Cæsarean section was not performed, as it is considered that the results of this operation in cases of hæmorrhage are not sufficiently encouraging to justify a departure from well-tried methods. Although there may be a small place for Cæsarean section in some cases of placenta prævia, as when the os is closed and the mother's condition good, there have been no such cases in this series. If all cases could be diagnosed before serious hæmorrhage has occurred, and treated under good hospital conditions, it might be possible to obtain a series with a death rate of 1% or 2%, but as many patients have no warning hæmorrhage and are too ill when first seen to bear removal, would it not be more likely for more lives to be saved if students were taught a method which can be safely performed after hæmorrhage and under the ordinary conditions of general practice? The nine cases of central placenta prævia in this series were treated as follows: Turning was done if the os admitted the finger easily and the toes of the fœtus were drawn through with tissue forceps, care being taken not to separate placental tissues while doing this operation.

As a precaution, in some cases the placenta was held with tissue forceps while being punctured, and the puncturing was usually done with a blunt instrument such as a uterine sound, and the finger was put through the hole thus made. If the cervix was so hard that it would not dilate sufficiently to admit of turning, placental tissue was separated as far as possible round the os with the finger, a quarter grain of morphia was given to the patient, and she was kept in bed until the os had dilated sufficiently to admit the finger comfortably, when turning was done. The nine mothers so treated recovered; the child was macerated in two cases, died during labour in four, and was alive in three.

A dangerous practice in cases of hæmorrhage is the undertaking of intra-uterine manipulations in a collapsed patient. This is never done at the hospital but the opportunity is taken to fill the axillæ with saline solution.

The use of saline infusions is considered of great importance. The routine is that as soon as a case of hæmorrhage is admitted, the labour ward sister prepares the apparatus and gets the patient warm, and when the doctor arrives the injection is begun, before any manipulation is undertaken.

Blood transfusion, even with the excellent facilities available in London, has proved of no value in these emergencies, as the treatment, to be effective, must be immediate.

Results to child.—The still-births were 50% (or 44%). Although version is usually considered dangerous to the child, it appeared in this series that death of the fœtus was determined rather by the amount of separation of placenta and the period of gestation than by the method of treatment adopted.

SEPSIS.

The hospital being a training school for midwives, the Central Midwives Board standard of pyrexia—namely, a temperature by mouth of 100·4° for twenty-four hours—is adopted. Table VIII shows that the number was 116 or 1·1%, while sepsis of the genital tract occurred in thirty-seven, or 0·35% (Table IX). This does not mean that temperatures under this are looked upon as unimportant; a case with a temperature of 99° only is always investigated by the doctor and the midwives are impressed with the necessity of seeing that they carry out this practice after they receive their certificate.

Analysis of the hospital cases in which definite sepis of the genital tract was diagnosed clinically or was assumed to be present, as no cause was found elsewhere, shows that the labour had been abnormal in 66%, and that in 33% the abnormality necessitated intra-uterine manipulation (Table X).

Relative incidence of pyrexia in home and hospital.—The incidence of sepsis was considerably less in patients confined in their own homes than in the in-patients', but as this might be due to the higher proportion of abnormal cases and primiparæ admitted, in Table XI the factors of primiparity and abnormality have been separated out. This shows that the incidence of sepsis following normal labour in multiparæ is practically the same whether the confinement takes place in home or hospital. The figures in primiparæ are hardly large enough for comparison, but it is significant that no district cases became septic.

The precautions taken to guard against sepsis appear to have been effective, but putting them down on paper conveys no idea of the daily and hourly watch that must be kept up by those in authority to ensure their being carried out.

Briefly they are as follows:—

(1) The hands are thoroughly scrubbed in hot soap and water for five minutes and then in perchloride of mercury, 1 to 1,000, for three minutes, a nailbrush being used to get into the crevices. They are frequently re-sterilized in the same way and always before a further vaginal examination is made.

(2) Special care is taken to avoid the predisposing causes of sepsis, which are considered to be trauma, exhaustion and hæmorrhage. The uterus is left empty of products of conception and of blood-clot.

(3) The patient upon admission has a hot bath and the external genitals are then swabbed with perchloride of mercury 1 to 2,000.

(4) The same care is taken during the puerperium as during labour.

(5) The reporting of any illness is enforced upon the nurses.

Neither gloves nor masks are used and aprons or gowns fresh from the wash are worn. In many cases as many as six different pupils make vaginal examinations.

Treatment of sepsis. (Table XII.)—In practically all cases in which there was a rise of temperature accompanied by such local signs as tenderness, delayed involution, or offensive lochia, and in some in which a slight rise persisted, although no local signs were present, an intra-uterine douche has been given, followed by digital exploration and removal of fragments, either by the finger or by the gentle use of a blunt curette.

Twenty-five out of the thirty-one cases of sepsis in the hospital were thus treated. It was usually done after the temperature has been raised for twenty-four hours, but in some cases it was delayed in the hope that the temperature would subside.

Exploration of the interior of the uterus has also been undertaken for sub-involution or secondary post-partum hæmorrhage without rise of temperature. (Nine cases.)

The number of cases in which this operation was performed was thirty-two, and in no case was there reason to regret having done it. Table XII shows that in

every case but one the temperature dropped to normal within forty-eight hours, and in no case was it followed by a further rise.

The operation was not performed in the few cases in which general infection was suspected.

These results do not confirm the general opinion as to the danger of this procedure. In fact, if any new treatment could show similar results, it would be at once hailed as a cure for sepsis. No such claim is made, but it is considered of value and free from danger. It should be realized, however, that the very greatest care and gentleness is required and that the operation should not be indiscriminately performed by those unfamiliar with the use of the curette.

Maternal Mortality.

(Table XV.) (A) In-patients.—(1) Septicæmia.—A difficult forceps delivery with extensive vaginal laceration. Pelvic peritonitis supervened and she was removed to a general hospital, where she died.

(2) Septicæmia.—A patient with abdominal pain and distension was admitted for observation. She was near full term and spontaneous labour took place next day, manual removal of the placenta being, however, necessary. Her temperature rose on the third day and on the thirteenth day she died from septicæmia.

(3) Septicæmia.—A patient who had had white leg in her previous labour twelve months before and who was still suffering from profound anæmia, neglected to book until fourteen days before labour was expected. At labour, manual removal of the placenta was performed. She again developed white leg and died on the twelfth day. Post mortem staphylococci were found in the thrombi.

(4) Syncope.—An elderly primipara was sent in by a doctor on account of valvular disease of the heart and a contracted pelvis. Induction was performed, but labour was more difficult than had been expected and forceps were required. She died from syncope two hours after delivery.

(5) Malignant endocarditis.—A patient admitted for bronchitis and toxæmia. The urine was stated to be solid with albumin. Induction was performed but her temperature rose the same evening. Malignant endocarditis ensued with multiple infarcts, and she died on the twentieth day after delivery.

(B) Out-patients.—(6) Syncope.—An elderly and obese multipara who died of syncope at the moment of an easy delivery.

(7) Malignant endocarditis.—A patient who was under the care of her own doctor for "influenza" died after a quick labour as the midwife entered the house. Post-mortem examination showed malignant endocarditis with numerous recent vegetations on the valves of the heart.

(C) Emergency Cases.—(8) Concealed accidental hæmorrhage.—The midwife was called by a doctor not connected with the hospital to a patient with concealed accidental hæmorrhage. The patient was collapsed. She was delivered alive but died from post-partum hæmorrhage.

(9) Hyperemesis.—A case of hyperemesis, three months pregnant. After one week of palliative treatment the uterus was emptied. She died in coma.

(10) Abortion with concealed hæmorrhage.—The midwife was called to a primigravida twenty-four weeks pregnant, who had been applying thermogene to the abdomen for a week on account of intense pain. She sent her to hospital at once, where concealed accidental hæmorrhage was diagnosed. Delivery took place in a few hours and eight pounds of blood were found in the uterus.

The causes of death were thus:—

In-patients:	Sepsis	4
	Syncope (difficult labour)	1
Out-patients:	Syncope (normal labour)	1
	Endocarditis	1
Unbooked cases:	Hæmorrhage	2
	Toxæmia	1
	Total ...	10

In the five booked cases the patients died from puerperal causes, giving a maternal mortality rate of 0·48 per thousand. The two deaths among the out-patients were due to incidental disease. Including these the rate is 0·67 per thousand.

Looking back upon the cases, it is easy to suggest that the treatment adopted was not the best possible, and it is indeed quite likely that were the cases to be repeated, the treatment would be different and possibly have given a happier result. It is encouraging to find that there were no deaths from eclampsia, from hæmorrhage in booked cases, or from sepsis following normal labour, and that the only deaths occurring among out-patients were due to incidental disease.

Taking a broad view, however, it would seem that as six out of the seven patients who died, in the booked cases, were seriously ill before labour commenced, any further material reduction in the maternal death-rate already attained is to a large extent dependent upon an improvement in the general health of the mothers, and it is intended to take further action upon these lines.

Maternal mortality compared with that of the neighbourhood.—While comparison of the maternal mortality with that of England and Wales would be valueless, on account of the large local variations which exist, it is interesting to compare it with that of the two boroughs from which the bulk of the patients are drawn, but it is difficult to get rid of fallacies, and caution must be used in drawing exact inferences.

It has been shown that there is no selection on medical grounds, but it must also be considered whether there are any special social or other factors which influence the course of child-bearing among the women attended by the hospital.

The chief of such factors are considered by McKinley [4] to be as follows:—

(*a*) Primiparity ratio.—Primiparous births have a higher mortality rate than multiparous. No official figures for primiparity rate are available for England but the Aberdeen inquiry found it 23 per cent. The percentage depends upon the birth-rate, and as this is high [5] in Poplar (20) and Stepney (22) the percentage of the hospital cases (24) is probably not very different form that of the two boroughs.

(*b*) Illegitimacy, with its high death-rate, is excluded from the hospital, but as illegitimate births from only 3% to 5% of the whole, the effect of its exclusion must be very slight.

(*c*) Social status.—The patients are poor, the wives of unskilled labourers, and in this do not differ from the surrounding population.

(*d*) Age distribution of births.—Maternal mortality tends to increase with age, so that a low age distribution would favour a low mortality. In Table XIV the age distribution has been compared with that of England and Wales, as calculated by McKinley, and is found to be considerably lower. There is no reason to suppose, however, that in this it differs from the local population, there being a large number of early marriages.

Apart from these considerations, there is the possibility that in abnormal cases the patients intentionally select other hospitals for their confinement, but it is largely a tradition in the district that women should have their babies where they themselves, and perhaps their mothers, were born, so that this is not a factor of any moment, even if it exists at all.

Giving due weight to all these factors, the conclusion may fairly be drawn that the cases of midwifery attended by the East End Maternity Hospital are a true sample of those in the boroughs of Poplar and Stepney.

As the hospital cases do not include ectopic gestation, abortion and some other accidents of pregnancy, which, according to the Registrar-General's returns, account for 10% of puerperal deaths, the figures for the two boroughs have been reduced by this amount in the following table:—

MATERNAL DEATHS PER THOUSAND. PUERPERAL CAUSES.

East End Hospital	Stepney	Poplar
0·48	2·16	2·57

The death-rate among the hospital cases is less than one-fourth of that of the neighbouring population.

Note.—It should be explained that in the official death returns of health areas any deaths of persons occurring in hospitals are referred to the area in which they are ordinarily resident. The existence of a hospital, such as the London in Stepney, admitting dangerous cases from outside the area, does not adversely affect the death-rate.

The deaths in Poplar and Stepney are low, following what may be considered the law for London, namely, that the maternal death-rate varies inversely with the birth-rate. The influence of the East End Maternity Hospital, which attends one-quarter of all the births in the two boroughs, is to lower it still further.

Still-births and Neonatal Deaths.

This inquiry affords an opportunity of studying the effect of antenatal work and careful obstetrics upon the still-birth and neonatal rate. As abnormal conditions in the mother are causes of fœtal death, and such cases tend to be collected in maternity hospitals, the figures of most of them are useless for this purpose, and it is only from a large series of unselected cases such as these that material can be collected from which reliable deductions can be drawn.

Still-births.—The still-births in these cases were 2·7% of all births; the corresponding figure for England and Wales for 1927 was 3·5%, while for Poplar and Stepney the figures were 2·6% and 2·7% respectively. The official percentages are calculated upon the number of still-births *notified*, and therefore fall short of their true number. As the hospital figures represent the *entire* number, it is probably correct to assume that there is a small reduction [6].

It is somewhat disappointing to find that measures which were effective in reducing maternal mortality by 75% have not had more effect upon the still-birth rate. The classification in Table XVI shows, however, that in 214 out of the total of 275, the cause of the still-birth was entirely beyond the influence of antenatal or obstetric care, and it was only in the remaining sixty-two that improvement could be hoped for by these means. The avoidable causes number 15% of the whole, as compared to Eardley Holland's findings that 51% of all still-births are preventable by good midwifery. [7] From these percentages it would seem that there has been a considerable improvement in the preventable still-births.

Neonatal deaths.—As the patients leave hospital at the end of fourteen days, only deaths occurring within that period are recorded. They numbered 135 or 1·3%. No British figures of the death-rate during the first fourteen days of life are available, but the Registrar-General's figures for the first week of life are given as 2·3% and for the first four weeks as 3·2%.

In the recently published "Child Life Investigations" by Cruikshank, it is stated that in a series of 800 deaths of infants within the first four weeks, 89% died in the first two weeks and only 11% in the third and fourth weeks. If this distribution be applied to the Registrar-General's figures, the rate for the first fortnight would be 2·8%.

It appears from these data that the neonatal deaths of the hospital cases are about one half the expected number.

In *Table XVII* the deaths have been divided into groups according as the cause of death operated before, during, or after, birth.

It will be seen from this that in neonatal deaths, as in still-births, the number due to causes at present beyond our control is large, forming here a percentage of 1·1 of all births. Antenatal care would have no effect upon their reduction, but the effect of care at birth, especially in the extraction of breech cases and in the management of asphyxia and care of the new-born child, has been to diminish the avoidable deaths to 24 or 0·24%.

It would appear that further knowledge of how to avoid intra-uterine death of the fœtus, premature expulsion and malformations, is necessary if the combined still-birth and neonatal death-rate is to be reduced below 3%.

Summary and Conclusions.

This analysis of 10,376 cases of midwifery shows that it has been possible, even in the present state of our knowledge, to reduce maternal mortality by at least 75%, to diminish the still-birth rate, and to halve the number of neo-natal deaths.

It has been shown that the cases form an unselected sample of the child-bearing population of the neighbourhood and that they are not specially favoured by social circumstances.

There have been no deaths from eclampsia, nor, among the patients who received ante-natal care, from hæmorrhage. No patient died from sepsis following normal labour and not one of the 4,233 women attended in their own homes died from puerperal causes.

As six out of the seven "booked" patients who died were seriously ill before labour commenced, any further material reduction in the already low maternal mortality rate would seem to depend upon improvement in the general health of the mother, rather than upon the increase of knowledge or alteration in the methods of practice of the hospital.

The practice is based upon the development to their full extent of the preventive and conservative aspects of midwifery, and minute care is expended in obtaining the utmost value from such well-established methods as should be within the competence of every well-trained medical practitioner.

Stress is laid upon the necessity of care in breech deliveries, of the treatment of collapse in hæmorrhage and of a simple, practicable and yet efficient antiseptic technique. Early exploration of the uterus in local sepsis is considered of great value and Cæsarean section is resorted to extremely seldom.

Although adherence to the fundamental principles of the obstetric art has proved of great importance, a partial explanation only of the success obtained is thus afforded, the factors above all others to which it is felt to be due being the sympathetic co-operation which exists all through the work, between doctors, midwives, and patients, the carefully thought out organization and the keen interest taken in the work by all concerned.

The work of the hospital confirms the conclusion of the Departmental Committee on Maternal Mortality:—

"Generally speaking it seems clear . . . that the solution to the complex problem of maternal morbidity and mortality will be found in all-round tightening up and strengthening of each link in the chain of obstetric supervision, an increased watchfulness over all stages of pregnancy and labour, rather than in any single, arresting or comprehensive remedy."

Table I.—Antenatal Department.

Number of patients' visits to midwife	38,583
Number of patients' visits to doctor	5,540
Number of patients admitted for treatment	341

Among the complications treated were:—

Albuminuria:		
Primigravidæ	168	(5·8 %)
Multigravidæ	49	(0·4 %)
Admitted	104	
Pyelonephritis	20	
Purulent vaginitis and cervicitis ...	74	
Morbus cordis	96	

TABLE II.—DELIVERIES AND PRESENTATIONS.

	Hospital	District	Total
Mothers delivered	5,143	4,233	10,376
Primiparæ	2,502	363	2,865
Infants born	6,283	4,255	10,538

Vertex presentations	10,103	Brow presentations	9
Breech ,,	316	B.B.A. or born in ambulance	70
Face ,,	27	Cord presentation or prolapse	29
Transverse ,,	13		

TABLE III.—POSTERIOR POSITION OF VERTEX. (HOSPITAL CASES ONLY).

Spontaneous rotation and delivery	579
Spontaneous delivery unreduced	95
Spontaneous rotation; forceps delivery	32
Manual rotation; forceps delivery	50
Forceps delivery unreduced	5
Total	761

TABLE IV.—BREECH CASES.

Original breech presentations		535
External version performed	219	
Unsuccessful, left as breech for teaching or undiagnosed	269	
One of twins	47	
The cases delivered as breech were		316
Uncomplicated	192	
Extended legs	66	
Twins	47	
Ante-partum hæmorrhage	5	
Descent of cord	6	

Cases in which version was performed during labour are not included.

Delivery took place as follows:—

Spontaneous	256
Manual extraction	55
Forceps to aftercoming head	5

TABLE V.—ANALYSIS OF STILL-BIRTHS AND NEONATAL DEATHS IN BREECH CASES.

Still-births.

Not due to presentation being a breech:

Macerated fœtus	11
Malformation inconsistent with life	3
Prematurity (5 lb. or less)	7
Antepartum hæmorrhage	4
Toxæmia of mother	1
Cord three times round neck	1
Dead before labour (cause unknown)	1
	28

Possibly due to presentation being a breech:

Large child, small pelvis	4
Prolapse of cord	2
Born before arrival of attendant	3
Died during labour—no cause found	1
	10

Neonatal Deaths.

Under 5 lb. in weight	12
Hydrocephalus	1
Apparently healthy when born	2
Attributed to atelectasis	2
	17

Summary.

	Born alive	Still-born	Died
In-patients	196	25	11
Out-patients	82	13	6
Total	278	38	17

The still-births and neonatal deaths possibly due to presentation being a breech were 14 or 4·4%.

TABLE VI.—OBSTETRIC OPERATIONS.

Induction.

Contracted pelvis	63
Toxæmia	48
Heart disease	6
Post-maturity	5
Ante-partum hæmorrhage	2
Double uterus	1
Head fœtus	1
Total	126 (1·2 %)

Podalic Version

Antepartum hæmorrhage	27
Transverse presentation	4
Prolapsed cord	3
Flat pelvis	1
	35

Forceps.

Persistent posterior	87
Contracted pelvis	64
Uterine inertia	39
Oversize fœtus	21
Fœtal distress	25
Rigid soft parts	15
Antepartum hæmorrhage	8
Face presentation	6
Brow presentation	6
After-coming head	5
Cord complications	5
Fœtal deformity	2
Double uterus	1
Maternal disease:—	
Morbus cordis	9
Toxæmia	4
Other disease	8
	302 (2·9 %)

Manual removal of placenta or membranes	73
Cæsarean section	1
Craniotomy	0
Total obstetric operations	537 or 5·3 %

TABLE VII.—INTERFERENCE PER 1,000 CASES.

	East End Maternity Hospital	Hospital X.
Induction	12	228
Forceps	29	117
Craniotomy	0	3
Cæsarean section	0·1	19
	41·1	367

TABLE VIIa.—ANTEPARTUM HÆMORRHAGE.

Accidental	74	*Placenta prævia*	49
Primigravidæ	11	Primigravidæ	12
Multigravidæ	63	Multigravidæ	37

Treatment.

Rupture of membranes	45	Version	23
Expectant	19	Expectant	22
Immediate delivery, forceps	4	Leg brought down	3
Immediate delivery, version	3	Packing	1
Packing vagina	3		

Number of cases 123

TABLE VIII.—PYREXIA.

In-patients.

Puerperal

Septicæmia	1
Peritonitis	1
Cellulitis	1
Septic absorption	25
White leg	2
Mammary abscess	1
Hæmatoma	1
Eclampsia	1
No cause found	6

Non-puerperal

Influenza	11
Bronchitis	15
Tuberculosis	1
Gastro-enteritis	3
Pericarditis	1
Endocarditis	1
Rheumatism	2
Pernicious anæmia	1
Alveolar abscess	1
Excitement	1

Out-patients.

Septic absorption	6
Mastitis	6
No cause found	10

Bronchitis	7
Erysipelas	1
Smallpox	1
Other diseases	4

TABLE IX.—CLASSIFICATION.

Cause of pyrexia	In	Out	Total
Sepsis of genital tract	31	6	37
Sepsis elsewhere	3	6	9
Other puerperal cause	4	—	4
Independent disease	37	13	50
Cause unfound	6	10	16
Total	81	35	116

Total pyrexia ... ... 1·1%
Total sepsis of genital tract ... 0·35%

TABLE X.

Labour followed by Sepsis. (*In-patients.*)

Normal	12
Retained products removed during labour	7
Ante-partum hæmorrhage	4
Prolonged labour; early rupture	3
Forceps with trauma or hæmorrhage	3
Forceps without other complication	2
Hæmatoma of vulva	1
Pyrexia present before labour:	
Macerated fœtus 3	
Septic miscarriage 1	
No cause found 1	5
Total	37

TABLE XI.

Incidence of Sepsis. (1925-1928.)

	Hospital		District		Total	
	Cases	Sepsis	Cases	Sepsis	Cases	Sepsis
Normal Labour—						
Multiparæ	2,672	3	3,275	4	5,947	7
Primiparæ	1,769	8	294	0	2,063	8
Abnormal Labour—						
Multiparæ	170	7	74	2	244	9
Primiparæ	212	11	20	0	232	11

Incidence of sepsis following normal labour in multiparæ is:—
Hospital ... 0·11% District ... 0·12%

TABLE XII.

Exploration of Uterus for Pyrexia.

Temp. Rose	Explored	Method	Temp. normal	Result
2nd day	2nd day	Digital		Next day
3rd ,,	3rd ,,	,,	,, ,,	,, ,,
3rd ,,	3rd ,,	,,	,, ,,	,, ,,
3rd ,,	3rd ,,	,,	,, ,,	,, ,,
4th ,,	5th ,,	Curetting	,, ,,	same ,,
5th ,,	5th ,,	Digital	,, ,,	next ,,
6th ,,	7th ,,	,,	,, ,,	,, ,,
7th ,,	7th ,,	Curetting	,, ,,	,, ,,
7th ,,	7th ,,	,,	,, ,,	,, ,,
7th ,,	8th ,,	,,	,, ,,	,, ,,
8th ,,	8th ,,	Digital	,, ,,	,, ,,
8th ,,	8th ,,	,,	,, ,,	,, ,,
9th ,,	11th ,,	,,	,, ,,	,, ,,
10th ,,	13th ,,	Curetting	,, ,,	,, ,,
11th ,,	11th ,,	,,	,, ,,	,, ,,
11th ,,	11th ,,	,, (bled freely)	,, ,,	,, ,,
11th ,,	11th ,,	,,	,, ,,	,, ,,
14th ,,	14th ,,	Digital	,, ,,	in 48 hours
2nd to 6th day	5th ,,	,,	,, ,,	next day
3rd to 6th ,,	5th ,,	Curetting	,, ,,	,, ,,
1st to 6th ,,	6th ,,	,,	,, ,,	same ,,
1st to 7th ,,	7th ,,	,,	,, ,,	,, ,,
2nd day	2nd day	Digital	99	evening until 16th day

Exploration of Uterus: Temperature Normal.

Indication	No. of cases	Result
Subinvolution	6	No rise of temperature
Secondary post-partum hæmorrhage	2	,, ,,
Offensive lochia	1	,, ,,

23 febrile; 9 non-febrile cases.

TABLE XIII.—CAUSES OF DEATH.

In-patients	Sepsis	4
	Syncope (difficult labour)	1
Out-patients	Syncope (normal labour)	1
	Malignant endocarditis	1
Unbooked cases	Hæmorrhage	2
	Hyperemesis	1
	Total	10

TABLE XIV.—PERCENTAGE OF BIRTHS AT AGES

Age Group	East End Maternity Hospital	Census, 1921
15—19	2·8	1·5
20—24	26·5	18·3
25—29	30·2	28·1
30—34	19·5	26·5
35—39	15·0	17·5
40—44	5·6	7·3
45	0·4	0·7

TABLE XV.—MATERNAL DEATHS PER THOUSAND

Puerperal Causes.

East End Maternity Hospital	Poplar	Stepney
0·48	2·57	2·16

TABLE XVI.—CLASSIFICATION OF STILL-BIRTHS.

Unavoidable:		
(1) Death before labour; fœtus macerated		119
(2) Death due to malformation		10
(3) Death due to prematurity, often twin		35
Possibly avoidable:		
(4) Death due to antepartum hæmorrhage		50
(5) Death due to toxæmia of mother		7
Probably avoidable:		
(6) Death due to abnormality of labour or lack of skill in delivery ...		43
(7) Death due to lack of skilled assistance (B.B.A.)		8
(8) Cause of death not ascertained		4
Total		276

TABLE XVII.—CLASSIFICATION OF NEONATAL DEATHS.

Cause operative before birth:		
Prematurity	77	
Malformation	29	
Sclerema	1	
Melæna	3	
Syphilis	1	
		111
Cause operative during birth:		
Atelectasis and birth injury	16	
		16
Cause operative after birth:		
Gastro-enteritis	4	
Bronchitis	1	
Icterus	2	
Overlaying	1	
		8
Total		135

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Discussion.—The PRESIDENT said he was interested to note that Dr. Oxley, with scientific candour, had stated that in a neighbouring institution where the methods in vogue were substantially different from those employed by himself and his colleagues, the results, in terms of mortality and morbidity, were almost as satisfactory. He gathered that, whilst reference was made to benefit accruing from blunt curettage in certain of his cases with early puerperal pyrexia, Dr. Oxley would regard anything like routine curettage in puerperal infection as a dangerous procedure.

Mr. L. CARNAC RIVETT said that from his personal knowledge of the work of the East End Maternity Hospital he thought that the good work done was mainly the result of the continuity of control both on the medical and nursing side. The late Dr. Corner had established a tradition which Dr. Oxley was carrying on. Miss Anderson, the Lady Superintendent, inspired all the workers with enthusiasm, and the hospital owed much to her. With regard to Dr. Oxley's treatment of pyrexia, he (Mr. Rivett) did not think it was clear to the Section that Dr. Oxley explored the uterus digitally only, in most cases, and gently curetted in certain cases and, in all except four of his cases, on the day on which the temperature rose; in his (Mr. Rivett's) opinion, this was a vastly different thing to advocating curettage in sepsis, and was really only establishing free drainage. [In reply to a question as to how he accounted for the low forceps rate at this hospital compared with other hospitals, Mr. Rivett stated that he thought the commonest indication for forceps at many hospitals was the desire of somebody or other to see them applied for teaching purposes.]

Dr. J. S. FAIRBAIRN said that Dr. Oxley had mentioned various reasons for the wonderful results attained at the East End Maternity Hospital, but they could all be reduced to the fundamental fact that the practice of this hospital was based on the principle of securing normal function, and that it acted up to that principle. However much we might succeed in perfecting our technique, artificial methods would always be second best to physiological, and until something more than lip service was given to this principle our maternal mortality would remain stationary.

Dr. Oxley had given no credit to the women whom his hospital attended, whereas he (the speaker) regarded them as a self-selected type, the hardier type who choose the hospital midwives to attend them because they were confident they could do their own work themselves, and who only wanted the services of the hospital for reasons of economy and convenience, or in case of accident. Those in that area who could afford to do so hired a doctor to give them anæsthetics and shorten their labour artificially, and thereby raised the mortality of the district. There would be general agreement on the methods of the hospital, except with regard to curetting in puerperal infections, and on that matter his own experience was not so fortunate as Dr. Oxley's appeared to be.

Dr. J. WYATT said he thought that curetting the uterus in cases of local uterine infection was a dangerous procedure except in skilled hands. He himself had had over 500 cases of local uterine infection to treat in the North and South-Western Fever Hospitals and no intra-uterine manipulations had been performed with the exception of injecting sterile glycerine; all these cases had done well, some had taken some days to settle but were not seen until the infection had been present some days.

With regard to the cause of death when the fœtus was born macerated: at St. Thomas' Hospital, signs of syphilis were found in over 50% of the cases either in the fœtus or the parents.

Dr. G. W. THEOBALD said he agreed with Dr. Oxley that the best way to treat occipito-posterior cases was to give morphine and scopolamine to the patients and leave them alone. He thought, however, that curettage of the infected uterus might be an extremely dangerous manœuvre. He had treated a considerable number of cases of puerperal infection and had given up all interference with the uterus except in those rare cases in which obvious pus could be expressed, and in these he gave a simple intra-uterine douche.

[*May* 16, 1930.]

A Short Communication on a Case of Endometrioma.

By F. J. HECTOR, M.D.

THE records of this case of endometrioma, in a young single woman, cover a period of $8\frac{1}{2}$ years and are, I believe, of sufficient interest to warrant this communication.

The patient, aged 26, was admitted to Chelsea Hospital for Women for the first time in September, 1921, complaining of severe dysmenorrhœa. There was a fixed retroversion of a slightly enlarged uterus and laparotomy was performed by Mr. Giles. The uterus was held down by dense adhesions and the left tube and ovary were also adherent to the pelvic floor. The adhesions were separated and the left tube and ovary were removed. The uterus was ventrofixed. The pathologist reported that the ovary contained numerous lutein and follicular retention cysts and the tube showed chronic inflammatory changes.

Nine months later the dysmenorrhœa still persisted and there was considerable pain in the left iliac fossa, sometimes accompanied by vomiting and often incapacitating the patient. Mr. Giles performed a second abdominal sections and found that the uterus contained multiple small masses resembling fibroids; the pelvic colon was adherent to it. Subtotal hysterectomy was performed and the cervix was sewn across by two mattress sutures. A hard mass was then discovered at the base of the left broad ligament involving a portion of the left ureter, which was kinked and afterwards found to have been occluded. The mass was resected together with the involved segment of the ureter and an end-to-end anastomosis of the ureter was carried out.

No pathological report was made on the resected mass but the uterus contained a soft interstitial fibroid and the endometrium was thickened and showed a few polypoidal growths, one of which was examined microscopically and reported to be a benign adenomatous polypus of the endometrium. For four years there were no symptoms and the patient enjoyed excellent health.

In November, 1926, however, there began to be an offensive brown vaginal discharge which was bright red at monthly intervals. An almond-sized polypus springing from the left vaginal fornix was removed. The polypus was vascular and appeared to be undergoing cystic degeneration. Unfortunately no pathological report was made upon it.

There was no further hæmorrhage for eighteen months, when the same symptoms of vaginal discharged recurred. More than a year later three friable and cystic polypi were removed from the left fornix and there was now considerable induration of the left fornix and the upper portion of the left vaginal wall.

The polypi were found to be composed of endometrial tissue embedded in a fibrous stroma with a little muscular tissue. Several of the gland spaces were filled with blood.

The patient, whose general condition is not quite so good, still has some vaginal hæmorrhage which is increased at monthly intervals and there is a fixed plaque at the posterior portion of the left lateral fornix. The cervix is free from this and the utero-sacral ligaments are not involved.

Three applications of radium in a lead container have been made since February of this year, the last application being on April 14. The bleeding has now somewhat diminished and the indurated plaque appears to have decreased slightly in size. At the time of each application sections were examined histologically and they all show definite endometriomatous tissue with no evidence of malignant changes. There has been no apparent histological alteration in the tissue during the course of the radium treatment.

Clinical Section.

[*October* 10, 1930, *continued.*]

Abdominal Carcinomatosis, with probable Adrenal Involvement.—MAURICE A. CASSIDY, C.B., M.D.

A. W., aged 31, railway signalman.

Family history.—Parents, one sister, wife and child, all living and healthy.

Past history.—Has had no serious illness. Was medically examined on joining the Railway Company, and subsequently; nothing abnormal discovered.

History of present illness.—In June, 1926, complained of "rushes of blood to the face." July, 1926: all teeth extracted on account of pyorrhœa. September, 1926: much improved. Returned to work and remained at work, and in good health till May, 1928, when he was ill for two days, complaining of pain across the sacrum and front of the thighs, followed for several weeks by loose motions. Blood-pressure 140/90. Urine normal. June, 1928: returned to work. Remained well till summer of 1930, when he suffered from recurrent attacks of diarrhœa, flushing of the face and to a less extent of the body, and occasional swelling of the left foot and leg. Several attacks of frequent micturition. Recently, attacks of palpitation with dyspnœa. He remained at work until three months ago. His bowels may be perfectly normal for a week or more at a time, and then he has an attack of watery diarrhœa, with action of the bowels as often as every half hour, day and night. During these attacks there is often frequent painless micturition, urine being passed at least hourly.

Condition on admission to St. Thomas's Hospital, September 18, 1930.—Phenomenal flushing of face, much exaggerated during emotion or during a meal. Numerous dilated venules of recent origin over the nose and cheeks. Skin of trunk is usually of a mottled mauve colour, but here, too, there is a liability to sudden changes to a vermilion hue. An exceptionally brilliant tache appears slowly, lasts for a few minutes, and leaves a pallid zone of cutaneous vaso-constriction behind it. No whealing produced. A flush begins to appear 14 seconds after a scratch, developing into a well-marked flare in 45 seconds; in centre of flare, representing the actual scratch, appears a thin white line. Three minutes later the flare is still bright red, with the commencing appearance of a peripheral pallor which slowly spreads inwards for a period of ten minutes. The vaso-constriction does not altogether disappear till eighteen minutes after the scratch.

Down the left sternal edge there is a loud blowing systolic murmur, maximal near 4th left intercostal space. No thrill. Blood-pressure 150 systolic, 120 diastolic.

There is a hard, irregular epigastric tumour, which appears to be the liver. Right kidney easily felt and is enlarged. Left kidney and spleen not felt. Temperature usually subnormal. Pulse rate 90 to 108. Urinary measure, 30 to 73 oz. One short attack of diarrhœa shortly after admission. Micturition frequent, at least every hour day and night, and disturbs sleep. Sexual organs normal. No varicocele. There is a large mass in the pelvis, and, per rectum, one feels a dense stricture 2 in. above the anus, which will barely admit the finger. No ulceration is visible through the proctoscope. It feels as if the pelvis were filled with plaster of Paris.

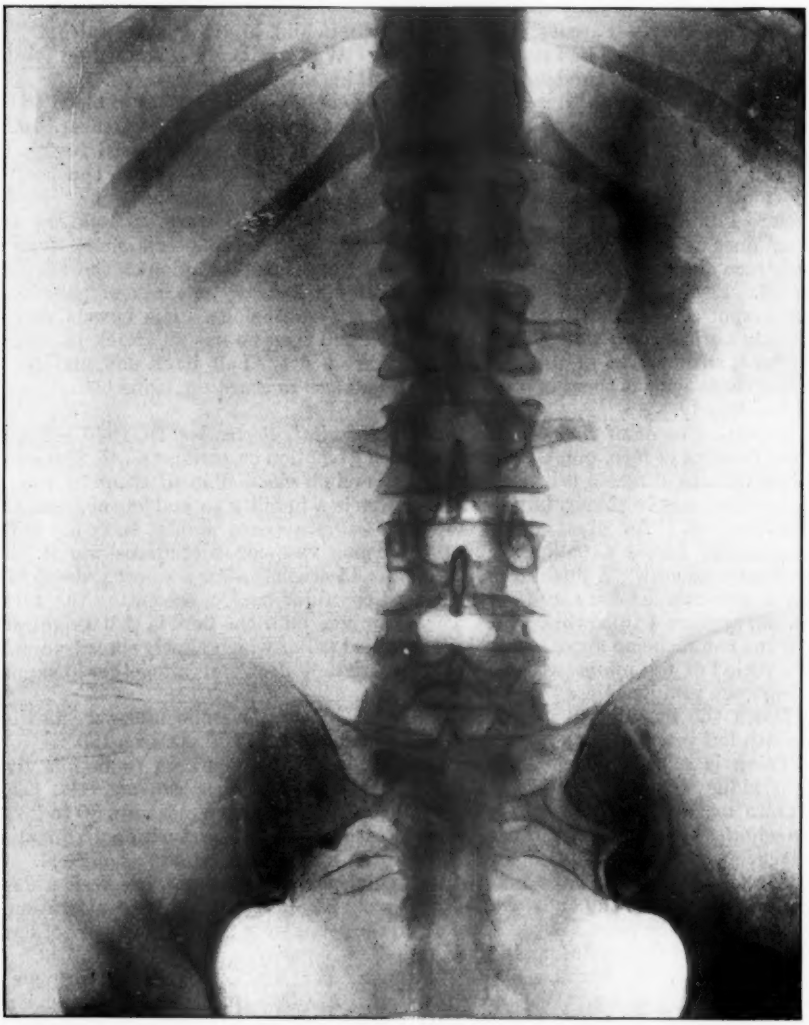
Loewi's test (adrenalin pupillary reaction).—Negative.

Blood-sugar.—4 hours p.c., 0·123 mgm. per 100 c.c. *Blood calcium.*—9·3 mgm. per 100 c.c. (Watford Hospital). *Electro-cardiogram.*—Pathologically flat "T" wave in all leads.

Urea concentration test.—First hour, 60 c.c. (1·5%); second hour, 80 c.c. (1·1%); third hour, 57 c.c. (1·0%). *Blood urea.*—75 mgm. per 100 c.c. *Sachs-Georgi.*—Reaction negative.

Blood-count.—R.B.Cs., 3,816,000; Hb. 76%; C.I. 1·0; platelets 373,800 per c.mm.; W.C. 12,000. *Differential count:* Polys. 75%; eosinos. 1·5%; small lymphos. 14·5%; large lymphos. 14·5%; large hyalines 8·0%; coarsely granular basophils 0·5%.

Bacteriology of stools.—*B. coli anaerogenes* the only abnormal organism found.
Urine.—Sp. gr. 1010. No abnormal constituents.
Radiogram of chest (6 ft.).—Lungs normal. Longitudinal diameter of heart 15 cm. Transverse diameter of heart 13·2 cm. Aorta not enlarged.



Skiagram 15 minutes after uroselectan. Shows slight dilatation of whole of left renal pelvis and calyces. No trace of excretion on the right side, which shows no kidney outline but a homogeneous shadow as from a solid tumour.

Uroselectan film report.—Excretion slow. Shows none on the right side, which has no kidney outline and is of homogeneous texture as of a solid tumour. The left side shows general dilatation of the pelvis and calyces in fifteen minutes. There appears to be some degree of obstruction of the pelvic outlet.

Showing multiple telangiectases and flushing on a previously cyanotic background.

MAURICE A. CASSIDY: Abdominal Carcinomatosis, with probable Adrenal Involvement.

UNIV. OF MICH.

The question is whether there is a carcinoma of the rectum, with secondary deposits in the liver, kidney and suprarenal gland. We may still think of the possibility that there is a primary suprarenal lesion and secondary deposits. The patient is intolerant of iodide of potassium, and it is too early yet to know the result of the administration of mercury. I think the heart murmur has become louder and harsher since he came into hospital, and I wonder whether there is secondary new growth of the heart itself. The persistent cough sounds mediastinal, but radiologically there is nothing to be seen in that region.

Gummatous Osteitis of Tibia.—C. E. SHATTOCK, M.S.

Patient, a boy aged 8, two months ago had a painful swelling of the right knee, which was red. This subsided and six weeks ago a swelling developed on the whole of the front of the leg.

Gummatous osteitis of tibia.

One week ago a localized "abscess" formed in the leg and this has increased in size.

On examination.—Fluctuating swelling fixed to tibia in upper part of leg. Not tender. Skin red and thin over the swelling. Tibial crest is rounded and bone thickened (see fig.). Knee-joint normal. No other signs of syphilis.

Wassermann reaction strongly positive.

Skiagrams show thickening and sclerosis of bone, with areas of rarefaction.

[*November* 14, 1930.]

True Hermaphroditism.—R. RUTHERFORD, F.R.C.S.

This child, aged 2, came under the notice of Mr. St. J. D. Buxton, F.R.C.S., in the summer of 1928, for the radical cure of a left inguinal hernia. Before operation it was remarked that the patient looked very like a girl (fig. 1). The penis was an inch long. Although the scrotum showed well-marked rugæ, no testes could be felt.

FIG. 1.—Photograph of child—note female appearance.

At operation, on opening the hernial sac, a uterus, Fallopian tubes and sex glands presented themselves. The relations of these structures to one another and also their appearances were those usually found in a female child of that age. A Fallopian tube and sex gland were removed for biopsy, and the sex gland found to be ovo-testis.

Microscopic sections show :—

(1) Testicular tissue and Fallopian tube tissue on the same block.

(2) The tunica albuginea invaded by cords of cells, amongst which are large cells having the appearance of primordial ova, with much clear cytoplasm and a well defined nucleus.

A drawing was made by Mr. Arthur Edmunds who was present at the operation (fig. 2). The uterus ends in lax cellular tissue; sex glands are attached to the broad ligament behind. Figure 4 shows the testis, tunica albuginea, tubules of the epididymis,

FIG. 2.—Drawing by Mr. Edmunds, M.S., F.R.C.S., made at the time of operation.

FIG. 3.—Photograph of external genitals after operation.

and Fallopian tube cut across four times. Histological examination of the testis shows seminiferous tubules which were not canalized, whereas they should be canalized, even in the fœtus.

FIG. 4.

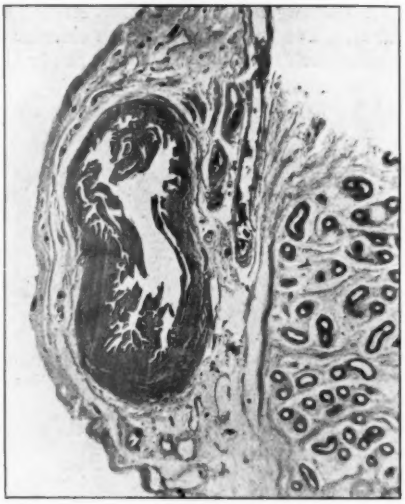


FIG. 5.

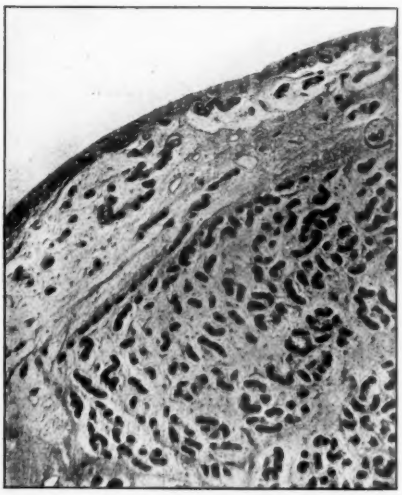


FIG. 6.

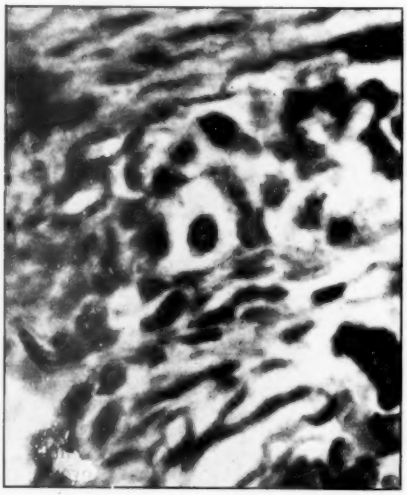


FIG. 7.

FIG. 4.—Photomicrograph of ovotestis × 3. Note Fallopian tube cut across four times.

FIG. 5.—Photomicrograph showing Fallopian tube and tubules of epididymis. (× 25.)

FIG. 6.—Photomicrograph showing periphery of testis. × 25. Note tunica albuginea invaded by cords of cells. (Compare Pflüger's tubules.)

FIG. 7.—Photomicrograph showing part of tunica albuginea. × 500. Note the primordial ovum or genital cell in the centre of the field, the surrounding stroma being a cord of cells (Pflüger's tubule).

One section, magnified 500 diameters, was taken from the tunica albuginea, and the specialized genital cells were evident, these cells being the type which is found lying in the Pflüger's tubules of the fœtal ovary.

This, therefore, is a case in which both male and female elements are present in a sex gland, and I submit it as an instance of true hermaphroditism, a condition which is extremely rare.

Discussion.—Dr. FELDMAN asked whether, in view of the structure of the sex gland which had been shown, it was possible for this child ever to become a father. The child's mother said he had very strong erections. The case was highly interesting in view of the fact that if the child had never been operated upon the condition would not have been discovered. It was conceivable that cases of sterility, due to undescended testes, might be of similar nature.

Mr. ST. J. D. BUXTON said that in this country the majority of patients who had double undescended testes came to the surgeon at some time because of hernia. The only case of true hermaphroditism in this country had been published by Sir George Blacker and Mr. Lawrence.

It was difficult to settle on an exact definition of a hermaphrodite. Strictly such a patient must have every organ of both sexes. Definitions of pseudo-hermaphroditism were very complicated. He thought that those who investigated such conditions would agree that a true hermaphrodite was one who had both male and female elements in one sex organ. Only one sex gland had been removed from this child. He had impressed on the mother that the child should be brought up as a boy. As far as one could tell at this age there was no likelihood of the uterus in this case menstruating.

Dr. F. PARKES WEBER asked how many genuine cases of ovo-testis were on record, and what happened later in those cases: did they develop secondary female sex characters? Was gynæcomastia known to have been associated with the presence of true ovo-testis in any case?

Dr. HUGH STANNUS said that he gathered from the histological evidence that this child appeared to be more male than female, and yet had a general air of femaleness. Were mammary glands likely to develop?

Mr. RUTHERFORD (in reply) said it was possible that the child might become a father. Two French authors quoted the case of a French soldier who was operated upon for a left inguinal hernia, and in the sac was found a uterus, with Fallopian tubes and sex glands, and he was the father of two children.

It was difficult to answer Dr. Stannus's question as to secondary sex characters. It depended on which was the dominant element: if the ovarian element, then he presumed the child would have female sex characters, and probably the uterus would menstruate. If the testicular element, it was doubtful if the child could become a father eventually, as it was suspected that the vas ended blindly. But he did not think it was justifiable to interfere with the uterus until the child arrived at puberty and showed symptoms of menstruation. The mother had been warned that if anything occurred she must bring the child to the hospital to be dealt with by the gynæcologist.

In answer to Dr. Parkes Weber, strange cases had been reported pathologically, and not long ago a female patient, aged 80, who was being treated for retention of urine, had a suprapubic operation performed, and it was found that she had an enlarged prostate.

He had gone carefully through the literature on the subject, and found that though many authors alleged certain tissue to be ovo-testis, the tissue had not been submitted to biopsy, and there had not been microscopical proof forthcoming.

Congenital Shortening of the Left Humerus.—A. D. MORRIS, M.B. (for CECIL P. G. WAKELEY, F.R.C.S.).

T. D., aged 45, is mentally deficient, and has been an inmate of institutions all his life. His left arm has been shorter than the right ever since birth.

Present condition.—The left upper arm is approximately half the length of the right one. The scapula follows all movements of the arm, the shoulder-joint being ankylosed. The left biceps and triceps muscles are functioning, and stand out

prominently as short, thick bands on the anterior and posterior aspects of the arm. The left forearm is of the same length as the right, and though the muscles are slightly wasted their motor power is good.

A skiagram shows the scapula to be narrower and slightly shorter than the normal one. The affected humerus is fairly normal in shape.

Congenital shortening of left humerus.

Is this a case of congenital short humerus? If so, how is the ankylosis of the shoulder-joint explained? On the other hand, is it possible that the joint was the seat of a pneumococcal arthritis in infancy, and that the shortening is due to interference with the growth of the epiphysis?

Discussion.—Mr. HAROLD EDWARDS said that the misshapen head of the humerus was lying underneath the acromion. The case was an example of congenital dislocation of the shoulder-joint, an extremely rare condition. He did not think anything should be done in the way of treatment.

Dr. HUGH STANNUS said that in five years he had seen seven or eight such cases among African natives. In only one case had he seen the lesion limited to one side. They had been published as cases of congenital shortening, but he had wondered subsequently whether they were really cases of epiphysitis in early childhood, possibly due to frambœsia or syphilis. In all his cases there had been deficient movement at the shoulder-joint, but it was impossible to say whether there was true ankylosis.

Spondylitis Deformans (Strumpell-Marie Type).—A. D. MORRIS, M.B.(for CECIL P. G. WAKELEY, F.R.C.S.).

P. O'M., aged 69, gave a history of having "ricked" his back in 1918, whilst carrying a heavy trunk up a flight of stairs. Following this accident, his lower limbs began to get stiff, and he was forced to give up his work. He has been an inmate of an institution for the past ten years.

Present condition.—His only complaint is that of stiffness of the hips, and of occasional pain across the back. He is able to walk with the aid of a stick. At the hip-joints the movements of abduction, adduction and extension are practically nil. A certain amount of flexion of the spine is possible.

Skiagrams show advanced changes of spondylitis deformans in the vertebræ, and marked osteo-arthritis of the hip-joints.

On account of his age, and the fact that he is able to get about quite well with the aid of one stick, and has very little pain in the hips, I think that no surgical treatment is required. If there was severe pain or inability to walk, would Sampson Handley's operation of cheilotomy be indicated in this case?

Discussion.—Mr. HAROLD EDWARDS said that a point of interest was the type of arthritis present in this case. He did not quite think that it was a true Strumpell-Marie type. The spine was affected in the lumbar region only. Both hip-joints were affected, and the most striking thing was that the arthritis of both these joints was painless. He wondered, therefore, whether it was a bilateral Charcot joint. There was an unusual amount of new bone formation in the hip. He did not recommend any treatment, except palliative measures.

Dr. F. R. B. ATKINSON said that the back was only affected in the lumbar region, and the arms had escaped, whereas in the "spondylose rhizomélique" of Strumpell-Marie the back was perfectly rigid and the arms, although not so markedly implicated as the legs, were always affected. The thorax also was rigid and the respiration entirely abdominal, whereas in the case shown, although the two or three upper ribs lagged, the rest of the chest expanded normally. He could not agree with the diagnosis.

Dr. F. PARKES WEBER did not think this case was one of Pierre Marie's "spondylose rhizomélique," as he believed that there was no genuine case on record in which the condition had developed so late in life, or in which, at the patient's age, the shoulder-joints were so little affected.

Bilateral Ankylosis of Hip-joints.—A. D. MORRIS, M.B. (for CECIL P. G. WAKELEY, F.R.C.S.).

H. S., aged 25, in 1919 had an accident in which he fell a distance of about nine feet. Following this, he complained that his legs "gave way," and he was sent into hospital. He was treated at one hospital or another practically continuously for about four years.

Present condition.—He is unable to walk without support. There is immovable fixation at both hip-joints, which are soundly ankylosed, and there is also ankylosis of the right elbow-joint. Over the region of the crest of the left ilium there are two old operation scars, and another over the lower end of the right humerus. The scars on the back are due to healed pressure sores.

Skiagram shows osseous ankylosis of both hip-joints.

Assuming that it is imperative to get a movable joint on one side in a case of bilateral ankylosis, should an operation such as arthroplasty be performed on one side? If so, which side is the more suitable for this operation? I take it that on the other side, then, a subtrochanteric osteotomy should be performed.

Discussion.—Mr. HAROLD EDWARDS said the history was one of trauma, but the skiagram showed, he thought, that the cause was arthritis. He did not know of an injury which would produce such osseous ankylosis as this patient had in both hip-joints; further each joint was subluxated slightly, and these facts fitted in with suppurative arthritis, or at least with arthritis rather than a traumatic affection.

In a young patient with both hips ankylosed, who was bed-ridden and unable to walk, operative treatment was essential. He suggested the performance of arthroplasty of one hip-joint, followed by an osteotomy on the other side.

Mr. E. G. SLESINGER said it was essential that something should be done for this man. Certainly arthroplasty on one side was indicated; he could not understand why the case had been left untreated so long. The infection seemed to have subsided, and the outlook for an arthroplasty was good. Then after the patient's progress had been observed the other joint could be dealt with accordingly.

Dr. W. FELDMAN asked why, if arthroplasty could be done on one joint, it could not be done on both. [Mr. SLESINGER: There is not so much stability after arthroplasty as after osteotomy.]

Anæmia with Splenomegaly.—F. PARKES WEBER, M.D., and M. SCHOLTZ, M.D.

H. H., female, married, aged 45, English, was admitted to hospital on April 29, 1930, with a history of pallor and menorrhagia following a confinement 8½ years ago. The child from that confinement, who is still living, was the fourteenth of fifteen children, of whom ten are still living. The first child (living) is aged 29 years; the last, born three years ago, died at one year of age. Previously to the confinement 8½ years ago, patient had never been ill. She has never been out of England. No history of anæmia in the family.

On admission the patient looked pale and "puffy" in the face, not obviously jaundiced, but her blood-serum gave a strongly positive indirect (but negative direct) Hijmans van den Bergh reaction for bilirubin. No abnormal "fragility" of R.B.C. to graduated hypotonic sodium chloride solutions. The spleen was enlarged, reaching down to just below umbilical level; liver not obviously enlarged. Galactose test (40 grm. by the mouth) for hepatic function gave a scarcely abnormal blood-sugar curve; the urine collected for six hours after swallowing the galactose contained 1 % sugar. Blood-count (on admission): Hb. 34%; R.B.C. 2,008,000; C.I. = 0·75; W.B.C. 1,650 (metamyelos. 2%; polys. 78 %; lymphos. 18 %; monos. 2 %); anisocytosis and poikilocytosis. The urine showed some excess of urobilinogen. Otherwise nothing abnormal was discovered by examination of the thorax, abdomen and pelvic viscera. Brachial blood-pressure: 135/70 mm. Hg. No retinal hæmorrhages or white foci. No gastric achlorhydria. Wassermann reaction negative in blood-serum. No pyrexia. General improvement under liver and iron treatment. Blood-count (June 2, 1930): Hb. 77 %; R.B.C. 4,480,000; C.I. = 0·86; W.B.C. 2,200 (eosinophils 2 %; polys. 52 %; lymphos. 36 %; monos. 10 %). But when seen again on October 18, the R.B.C. count was slightly less (4,200,000), and the spleen, though not hard, could be felt reaching down to the anterior superior iliac spine.

In regard to the real nature of the anæmia and splenomegaly, Dr. Weber remarked that if there had been a decidedly diminished resistance of the erythrocytes to graduated hypotonic sodium chloride solutions, he would not have hesitated to

diagnose the case as one of hæmolytic jaundice, in spite of there being no familial history. It was however now known that in even decidedly familial cases of what had to be regarded as hæmolytic jaundice, increased fragility of the red cells was not invariably present.[1] Nobody could, therefore, point to absolute evidence that this case was not one of hæmolytic jaundice without a familial history, and at present without increased fragility of erythrocytes.

Simple Achlorhydric Anæmia (L. J. Witts).—F. PARKES WEBER, M.D., and M. SCHOLTZ, M.D.

G. D., female, married, aged 52, English, came to hospital in July, 1930. Menopause five years previously. A pale woman, of medium size and weight, without any obvious jaundice and without any enlargement of liver or spleen. No particular "smoothness" of the tongue. Blood-count (July 4): Hb. 31%; R.B.C. 2,740,000; C.I. = 0·6; W.B.C. 2,050 (eosinophils 1%; poly. 70%; lymphos. 27%; monos. 2%). Gastric achlorhydria, complete, even after a subcutaneous histamin injection. Blood-serum gives negative Wassermann and Meinicke reactions, and a negative direct and indirect Hijmans van den Bergh reaction for bilirubin. No excess of urobilinogen in the urine. Brachial B.P. (July 26): 135/80 mm. Hg. No occult blood in the fæces. Nothing abnormal by ophthalmoscopic examination.

Blood-count (in out-patient department, October 18, 1930, after treatment with iron and an acid pepsin medicine at meals): Hb. 76%; R.B.C. 5,150,000; C.I. = 0·74; W.B.C. 4,200 (eosinos. 2%; polys. 62%; lymphos. 27%; monos. 9%).

Anæmia of this type was well described by L. J. Witts in the *Guy's Hospital Reports* (1930, lxxx, pp. 253-296) under the heading "Simple Achlorhydric Anæmia." There have been other examples in women at the German Hospital. In an apparently similar case in a younger woman (Mrs. A. N.), aged 30 years, the achlorhydria (fractional tests, but not controlled by a subcutaneous injection of histamin) disappeared whilst the patient was under treatment for the anæmia. It is probable (as Witts suggests) that cases of the kind have been classed as "late chlorosis" by O. Naegeli (*Blutkrankheiten*, 4th edition, 1923, p. 281).

One recent case at the German Hospital, possibly of the same character,[2] was in a man (A. H.), aged 56, who had complete gastric achlorhydria (even after a subcutaneous injection of histamin) and a R.B.C. count of 3,700,000 (Hb. 40%; C.I. = 0·54).

Discussion.—Dr. L. WITTS said that cases of the kind were really common; he had notes of nearly seventy of them, and he thought they were nearly twice as common as cases of Addison's anæmia.

The prognosis in these cases was good, and it was infrequent to find them going on to the development of Addison's anæmia. They continued with a secondary type of anæmia, and though they might have splenomegaly and glossitis, they never developed subacute combined degeneration of the spinal cord.

Dr. Parkes Weber had mentioned a case in which the achlorhydria had disappeared under treatment. In his (the speaker's) experience that was a new observation, because many of his own cases had had further test-meals at intervals extending to ten years, and the achlorhydria had persisted. He had had cases with achlorhydria alone, in which anæmia had developed later; also cases in which the anæmia developed after gastrectomy or after gastro-enterostomy. There was evidence, therefore, that achlorhydria was the primary factor, and anæmia developed as a secondary result. When the anæmia had been cured, the achlorhydria persisted. For this reason this case of Dr. Parkes Weber's was an important one.

1 See, for instance, the familial series described by C. Evans, *St. Bart's. Hosp. Journ.*, London, 1930, xxxviii, p. 25, and the references given by F. Parkes Weber, *Proc. Roy. Soc. Med.* (Children), 1930, xxiii, p. 19.

2 Compare, however, D. T. Davies and T. G. I. James, "Achlorhydria and Anæmia in Advancing Years," *Lancet*, 1930, ii, p. 899; also same authors, *Quart. Journ. Med.*, 1930, xxiii, p. 1.

Mr. A. DICKSON WRIGHT asked whether the exhibitor found any difference in the flora of the stomach in achlorhydric anæmia, because in cases of anæmia after gastrectomy the bacteriology of the stomach was changed considerably and anaerobic organisms were discovered. It had been suggested that, owing to organisms living at a higher level in the alimentary canal, a toxin was caused which produced the anæmia.

Dr. JANET VAUGHAN asked whether the exhibitor had had the opportunity of finding out whether these patients had a peculiar dietary history. She had seen several cases of achlorhydria associated with anæmia in which the patients admitted having eaten no meat or green vegetables for several years. It was possible that the absence of free hydrochloric acid led to indigestion, that the patients limited their diet in the hopes of improving digestion and that owing to the lack of iron-containing foods anæmia resulted. Such cases responded extremely well to iron alone, no hydrochloric acid being given, suggesting that the anæmia was due to a dietary deficiency rather than to achlorhydria.

Dr. PARKES WEBER in reply said that the stomach flora had not been specially examined. He suspected that some of these cases would do almost equally well with iron and without the acid, although he had not tried it.

Dr. WITTS said that he had not examined the intestinal flora as a routine in his cases, but in several the duodenal tube had been passed, and an abnormal number of bacteria had been found, yet the patients had recovered under treatment with iron. Many of these women patients were taking diet containing little or no red meat. His own opinion was that this was an iron-deficiency disease, to which these people were particularly liable, partly because of their abnormal diet, and partly because, in the absence of acid from the stomach, iron was not so well absorbed by them as in people with a normal gastric secretion.

? Syphilitic Osteitis of Humerus.—HAROLD EDWARDS, M.S.

Patient, female, aged 18. For twelve months has had pain in left shoulder, aggravated by movement. Has had to give up work for the last six months, and has lost 2 stone in weight since the onset of the pain.

Condition on examination.—Marked wasting of muscles over left shoulder-joint, and tenderness over greater tuberosity of humerus. Movements are painful and limited, especially abduction.

Skiagram shows rarefaction at upper end of humerus, and laying down of new bone under periosteum of upper end of shaft.

Wassermann reaction, positive.

The report of other cases shown at this meeting will be published in the next issue of the PROCEEDINGS *of the Section.*

Section of Medicine.

President—Dr. R. A. YOUNG, C.B.E.

[*October* 28, 1930]

DISCUSSION ON RESEARCH IN CLINICAL MEDICINE.

Dr. J. Ryle: I presume that the main motive for an open debate on research in clinical medicine is a prevailing sense of dissatisfaction with the present achievements of clinical inquiry or with the conditions upon which achievement depends. I believe it is no exaggeration to say that we are all at this moment alive to the existence of disturbing and retrograde tendencies in modern medicine. In the department of diagnosis, early specialization and the advent of numerous physical and chemical methods, which at first promised—and in some degree have proved competent—to enhance the science and accuracy of clinical study, have brought disappointment in their train, have hampered the natural evolution of common observation and common sense, and fostered faulty methods and an uncritical attitude in experiment. In the department of therapeutics, although there have been some notable discoveries, the same uncritical attitude and commercial enterprise have between them encouraged an empiricism quite unworthy of our age. In the department of prognosis there has not only been no general advance, but an actual loss of competence through neglect of the study of what may be called the natural history of disease in man. The time has come for a reawakening of interest in medical philosophy. Clinical practice will receive a strong stimulus to improvement when the methods of clinical science are better determined. It is a part of the function of philosophy to determine method.

Apart from a general and largely silent discontent there have also been two important pronouncements of late which I cannot but hold responsible in some part for the inauguration of this discussion. I refer to papers by Sir Thomas Lewis on "Research in Medicine, Its Position and Its Needs" (*Brit. Med. Jour.*, March 15, 1930), and by Mr. Wilfred Trotter on "Observation and Experiment and their Use in the Medical Sciences" (*Brit. Med. Jour.*, July 26, 1930). I am sure that many, like myself, must have drawn inspiration from these papers and that there is much to be found in them on which to base the general scheme of our discussion. More recently, and since my own thoughts were put to paper, Lord Moynihan has handled the same topic in his address at the Banting Research Institute.

My first duty as opener is to indicate the boundaries of the subject, and to suggest what aspects of it we may most profitably consider. I would suggest that we might consider in turn the meaning, the methods, and the scope of modern clinical research

and the opportunities which are at present, or should ideally be, provided for its proper conduct.

The meaning of clinical research.—Of the department of progressive medicine whose needs he is voicing, Sir Thomas Lewis writes: "It may be termed *clinical science.* This science seeks, by observation and otherwise, to define diseases as these occur in man; it attempts to understand these diseases and their many manifestations, and here especially makes frequent use of the experimental method. It makes definite experiments upon disease or watches the effects of experiment conducted by injuries, however these arise; it culls, or actually creates, and uses physiological and pathological knowledge immediately related and applicable to the diseases studied. Its value has been abundantly and frequently displayed in this country by such experimental clinicians as Ferrier, Horsley, Mackenzie, and Head. The very mention of these names is in effect a definition of the science that is in mind. Their work was not work that could be delegated to laboratories; it was inspired and sustained by direct contacts with disease; it was carried through in very large or chief measure by observations on sick people."

In defining the meaning of clinical research we cannot, I think, do better than follow this lead. Research in clinical medicine is not pathological, bacteriological, or biochemical research. These are concerned with the study of the agents, the processes and the consequences of disease in man under the conditions of the laboratory, and often with the help of experiments in animals. Clinical science should rather be considered as a branch of the science of human biology. It studies the behaviourism of disease in man, or perhaps it would be more correct to say of man in disease. It observes, records and, when possible, measures the processes of disease as they occur in the living subject, and within certain limitations it may control, modify or reproduce these processes for purposes of detailed study.

The methods of clinical research.—The methods of all scientific research, in their broadest subdivision, are either observational or experimental. Some sciences, such as astronomy and geology, are essentially observational. Others, such as physics and physiology, have depended for their progress almost entirely upon experiment. The great scientists like Harvey and Darwin have wherever possible employed both methods, calling one in support of the other. While it was a particular instruction of Harvey's that we should "search and study out the secrets of Nature by way of experiment," in all his work and elsewhere in discussing method he couples observation with experiment knowing them both to be indispensable in the biological sciences and complementary to one another. The great clinical scientists have all realized this, but with the growth of the ancillary sciences of physiology and pathology the natural tendency has been in the direction of a division of labour, the demands of experiment claiming certain faculties and an expenditure of time which left little opportunity for observational study, and the busy life of the physician (the student of φύσις or nature, as his name implies) allowing small scope for experiment. Scientifically it has been the misfortune, not the fault, of the physician that he has always had to expend a disproportionately large part of his energies in the treatment and management of patients. As Lewis insists, the pursuit of curative medicine necessarily conflicts at many points with the advancement of scientific medicine. Nevertheless many of the greatest contributions to medicine—or shall we call it physic, the science of the physician or naturalist?—have been due to members of the observational school who were practitioners of medicine. Hippocrates, Sydenham, Bright, Laennec, and Addison were among the foremost exponents of this school and, although he cites them as examples of the experimental clinician, I am sure Lewis would admit that Ferrier, Mackenzie and Head owed at least as much of their achievement to the method of observation.

In medical biography it is interesting to note how frequently able physicians have been able naturalists in other branches.

Both Lewis and Trotter in the papers referred to would seem to imply that the great and spacious days of observational medicine are almost numbered and that the future is all for experiment. Here I cannot find myself in full agreement with them. With improvements in our methods of training and observation, I believe it should be possible to add to our knowledge of man in disease contributions as important as any of those made in the past and often equivalent in practical advantage to those supplied by experiment. Further, whereas the fields open to the observational physician—difficult though they be to encompass—are many and varied, the scope of experiment must, by the dictates of humanity, remain somewhat strictly limited.

At this point, perhaps, we should demand a clear ruling as to where observation ends and experiment begins. The use of instruments of precision, for instance, cannot be held to turn observation into experiment. The stethoscope, the sphygmomanometer, the electrocardiograph have all improved our observational capacity, but to study a patient or a series of patients with their aid constitutes not an experiment but a refinement of the observational method. The same may be said of radiology and the innumerable biochemical tests which have for their purpose the measurement of vital phenomena and their comparison with normal standards. If on the other hand we study the effects of a new drug on the action of a disordered heart with the aid of the electrocardiograph; if we strive to reproduce a gastric pain artificially and simultaneously observe the movements of the stomach on the fluorescent screen; if we watch the capillary responses to applications of heat or cold or the injection of a drug; if we invent a new operation; then we are employing the experimental method. In the one case we are observing the casual experiments of nature; in the other we are actually promoting small-scale experiments of our own.

When we come to a consideration of the projects and the more intimate procedures open to the observational physician and to a comparison of these with those at present available for the experimentalist I think we must agree that the former still has the broader programme before him. Just as in animal biology the modern trend is in the direction of studying behaviour, œcology, and genetics in the open, as opposed to laboratory inquiry, so in my belief the next trend in clinical medicine (or the biology of man in dis-ease) will be in the direction of a study, at once broader and more intimate, of behaviour, personality, idiosyncrasy, vital reactions and genetic factors in our living patients, while experimental inquiry (always, I trust, co-operative), in the hands of an expert few, runs a parallel if somewhat subsidiary course. Until new instruments of precision come to trial, or some new departure in pharmacology or surgery is signalled, the methods of human experiments at our disposal are, it seems to me, conspicuously few.

The scope of clinical research.—The contributions of the older physicians were chiefly in respect of the broader natural history of disease. By careful study of symptoms and signs and at a later date by correlation of the phenomena observed in life with the changes found in the cadaver, they established a classification of diseases and some reasonable interpretations of symptoms. They also paid much attention, though of a superficial kind, to the influence of temperament, heredity and environment. They often wielded well the tool of inductive reason. In their tasks they were chiefly hampered by their limited knowledge of normal physiology and by their lack of precise methods of observation. Later generations have recovered the ground they trod, adding and improving here and there by new and more accurate observations, or by the interpretation of old observations on the basis of fresh physiological and pathological knowledge. New diseases continue even now to be

discovered and described by the observational method. A more minute analysis of morbid phenomena continues to make our appreciation of the natural history of the old diseases more intimate. Where laboratory research has had an application this has generally been promptly utilized. Where laboratory research has led astray or has endeavoured to simplify when simplification was impossible, the clinical observer has often supplied the corrective. I would maintain that his task is not nearly ended.

Certain special fields for clinical research at once commend themselves. The wide realm of subjective symptomatology, which constitutes a major part of morbid physiology—and, let it be remembered, symptoms are the earliest phenomena of disease—is still largely unexplored, if we except certain important contributions to the study of pain. We ought by now to have more accurate information in our possession about nausea, heartburn, the dyspnœas, and the many varieties of aches in body, head and limb. It should be possible to determine with greater precision the nature of those abdominal pains which nowadays lead so constantly to fruitless surgical intervention. Symptoms as expressing particular disturbances of function and not as listed characteristics of a particular disease are clamouring for organized research. The influence of constitution on the incidence and course of the chronic diseases is just beginning to attract fresh interest which should go far to provide a stimulus for future research, not necessarily along the anthropometric lines laid down by Draper. In therapeutics there is much waiting to be done, but almost more to be undone. It should not have been necessary to wait a quarter of a century to discover by slow and bitter experience that the greater part of vaccine-therapy as prescribed or practised by specialists having little or no acquaintance with the natural history of disease in man was a delusion unworthy of a scientific profession. With combined experiment and observation in accredited hospitals by trained workers it should be possible to decide within a comparatively short time what is good and what bad in the serum treatments and chemotherapies at present advocated in acute bacterial disease, and what is potent and what useless among the endocrine preparations. The principles of prognosis in acute bacterial infections and other anxious maladies should by careful observation become more surely established. Neurology has in recent times been greatly and rapidly advanced mainly by observation, but partly also by surgical experiment. In the realm of morbid psychology, which owes all its rapid growth to the observational method, there is ample scope for further research, and by this means many diseases and disorders at present in receipt of vague physical labels will eventually find their true home.

I have mentioned but a few departments of medicine awaiting the broom of careful observational research. In several instances experiment should lend a helping hand. In each instance it seems reasonable to hope that research will bring practical advantage. But clinical research need not necessarily be utilitarian. There are many diseases of obscure causation which are worth studying for their own sake as natural phenomena. Much research in modern physiology is devoid of immediate application, and for those who have no humanitarian interest in medicine and can devote their lives to such work clinical science can also provide a wealth of problems. Among the rarer diseases and peculiarities there are some which may provide for the experimentalist material especially suited to his needs.

The opportunities for clinical research.—We come lastly to the question of opportunity. There can be no disputing the truth of Sir Thomas Lewis's contention that at present there is no adequate provision and no adequate encouragement for the young man who would devote his life, or part of it, to clinical research. The stepping-stones whereby he must cross the stream between qualification and economic independence in medicine are customarily house-appointments, junior staff appointments, and for a shorter or longer period of lean years, an assistant

physicianship at a teaching hospital. Alternatively he makes general practice or specialism his goal. If he embark during any part of his probationary period upon a useful piece of research he is seldom if ever in a position to give it his full time or to find free access to the appropriate material. As a rule he does not see enough patients. As soon as practice—which is the necessary aim—begins to arrive his outlook alters, his time is consumed, and his hopes of scientifically productive work diminish. A research grant may help him here and there, but no one and no institution offers him security. Physiology and pathology, none too well endowed themselves, offer better economic opportunity than clinical science.

It is doubtful, however, whether "curative" medicine and "progressive" medicine, as Lewis calls them, can ever be divorced as he would wish. No one can conduct research on patients who are not under his own care, and no one can have patients under his care for research purposes and not treat them. It should, however, be possible for a promising man to be relieved of the absolute necessity of private practice and much crippling routine for a term of years, and, in special cases, through his working life. The professorial units with their assistantships do not quite fulfil the requirements. Special hospitals or wards for selected men and devoted to research purposes would defeat their own ends through creating a wrong environment, a new kind of ultra-specialism and a separation from the healthy criticism of men engaged in teaching and practice.

In the scheme for research physicians as at present forecast by Sir Thomas Lewis and the Medical Research Council there are many points for criticism but there is the germ of a good idea. To become a physician at all (whether we use the term in its oldest and best sense as meaning a student of nature, or in its modern interpretation as a healer of the sick) requires many years of initiation in a school far harder than the schools of physiology and pathology, involving constant contact with large numbers of patients. Only from such experience can fruitful ideas and a proper balance be derived; there is no short cut. Yet Lewis requires that his men should be young and that they should be relieved, from the beginning, of the gruelling apprenticeship of out-patient work and ward-teaching and forbidden that intimate school of private practice wherein most of us find our opportunities of seeing disease in its earlier stages and more active phases, of examining intelligent patients under favourable conditions of privacy and in their natural environment, and so of gathering, in my firm conviction, our richest crumbs of instruction and inspiration. Personally I should like to see a vacancy declared from time to time at the teaching hospitals for an additional assistant physician, the appointment to be an open one and filled only if a man of outstanding merit is forthcoming. The post should supply a general medical out-patient day, a few beds, and access to all material in the hospital of use to his self-instruction and research; with certain definite restrictions in respect of time and fees, and (except in the case of acute disease) within the precincts of the hospital, he should be allowed to see private patients referred to him by colleagues familiar with his interests and his needs; the appointment should be for five years in the first instance and then either renewable indefinitely or convertible, perhaps, to an honorary assistant physicianship of the usual type; the salary should be commensurate at least with those accorded to men of junior professorial rank and in the event of continuance of the appointment, should rise to equal those accorded to full professors. Such a research physician, although probably chiefly concerned with one or two types of disease, must have access to all types, must work in an atmosphere of disease considered from all points of view, and must be in contact with senior, contemporary and junior colleagues willing and eager to help or criticize. Whatever previous training he may have had in physiological or other laboratory method he should have held, as an introduction to the problems of man in disease, house-appointments for a year or two at least, and for a period of not less than two or three

years, a medical registrarship or tutorship, or have served a like period at special institutional medicine or in general practice. In the selection of candidates credit should be given for a broad earlier education and particularly for some grounding in philosophy or psychology as against purely technical abilities or an uninterrupted scientific education from the school period. Qualities as physician or naturalist should be allowed at least as strong a claim as qualifications for research in other spheres. A scholarly heredity should, by Galtonian doctrine, be considered a very distinct advantage.

These matters deserve our serious consideration, and the more so because the Medical Research Council have awakened to the importance of clinical research and are prepared to lend it the help of their endowments. The problems which it is their desire to solve are our daily problems. It is natural that we should wish to see them wisely approached.

Professor Henry Moore (Dublin): Up to comparatively recent times clinical investigation of disease consisted, in the main, of bedside observation aided by relatively simple tests and quantitative measurements, together with an attempt at the correlation of symptoms and faulty function with the structural post-mortem and post-operative changes found in organs and tissues—the observational method, we may call it. It was, is, and always will be, a productive method of research, and it has a most important function as the testing ground of discovery. During the past score years there has been a progressive increase of interest on the part of clinicians in the functional, as well as in the structural, aspects of disease, with the result that not only have pathology and physiology become enriched, but a better and more fundamental understanding of disease processes is being gradually, if slowly, obtained. In other words, we have come to think of disease in terms of physiology, that is, in terms of the living organism. The study of these more detailed and intricate aspects of disease necessitated methods more searching than mere bedside observation alone; thus, the more precise and quantitative methods of the laboratory and the experimental method for the testing of hypothesis, involving the use of animals if necessary, came to be made use of in the clinic. This resulted in the necessity for clinical investigators to train themselves in the use and the interpretation of the more advanced methods of the laboratory, in order to employ them in their quest of the elucidation of disease problems in the clinic. The clinicians themselves transported the technical methods and procedures of the laboratories to the clinic, and used them as important adjuncts, wherever necessary, for the active study of disease as it occurred in the victim himself, that is, in its natural environment. This is one of the key-notes of organized modern clinical research; the method continues to yield progressively rich results, As a consequence of the wealth of information thus accumulated and of the truly enormous literature which resulted (not all of it, I fear, quite sound), modern medicine has become one of the most complex and difficult of the sciences, while still retaining its old character as an art. It is a healthy sign of clinical medicine that those who practise it have become dissatisfied with the explanation of disease processes offered from laboratories which themselves have only the most indirect contact with disease as it naturally occurs. Who is more fitted to study disease than the clinician, the man who observes and handles it all his days, provided that he is able to use all the available weapons of attack, that is, both laboratory and clinical? Where should it be studied other than as it naturally occurs, in the patient? No one, certainly, who has frequent contact with disease will deny that the study of the patient is important and fundamental, and that it will yield much useful information in the future, as it has done in the past; but, as our knowledge

progresses, or as our lack of it is revealed, problems too complicated to be solved by clinical observation alone manifest themselves, and thus the more precise and complicated aids and instruments of precision of the laboratories, including animal experiment, become necessary as important adjuncts in the clinic for their solution.

By way of illustration, let us briefly consider some of the more important advances of recent years in clinical medicine. Recall to mind the complicated combined biochemical and bedside studies which gave us our present understanding of acidosis, ketosis and diabetic coma, and of the principles underlying the dietetic treatment of diabetes mellitus. Insulin, which probably has saved more lives and given more comfort to the human race since its introduction than almost any other drug in the same period, was discovered, it is true, in the laboratory, but it had to be subjected to an intensive co-ordinated study in the clinic and laboratory before it could be intelligently used in the treatment of diabetes and diabetic coma. The discovery of the extraordinary property of liver which enables the erythroblasts of patients suffering from pernicious anæmia to maturate—based admittedly on the laboratory work of Whipple on dogs rendered chronically anæmic from repeated hæmorrhages—was made in the clinic, and was elaborated in a careful, scientific, laboratory-clinical study, which may well be pointed out as a classical example of how clinical research should be done. The same close co-operation between bedside and laboratory work is seen in the discovery of the pre-operative use of iodine in toxic goitre and in much of our recently acquired knowledge of diseases of the heart, certain diseases of infants and children, some diseases of the gastro-intestinal tract, our partial understanding of certain aspects of immunology and the treatment of certain infections, the differentiation of certain types of nephritis, the discovery that the secretion of the normal stomach can form from meat a substance as potent as liver in inducing a remission in pernicious anæmia, and in other branches of progressive clinical medicine too numerous to mention. Indeed, one may say that the first harvest of the results of the method have scarcely yet been fully garnered, so fruitful has been the sowing. It is not unimportant, also, that the co-operative clinical and laboratory method has frequently disproved false claims and saved us from wasting valuable time and effort in following inefficient and unscientific procedures. Thus, we see that a considerable proportion of the advances made in clinical medicine in recent years—discoveries of such importance that they have profoundly changed the practice of medicine in the last two decades—have resulted from the co-operative working of the clinic and laboratory as one unit. In fact, the majority of the clinical investigators of to-day must not only be trained for work in the wards, but be prepared to perform, supervise, or advise upon the procedures of the laboratory in relation to the solution of their clinical problems. This is the main and the significant fact to which we must give recognition in this discussion. Of course, it is not suggested that every clinical investigator must necessarily work in the laboratory, or that every laboratory worker must actively participate in bedside observation, but if the signs of the times are correctly interpreted in this matter, there seems to be no doubt that the closest co-operation is necessary between the laboratory and clinic, and that, in clinical research, those who work mainly in the one should be, in some degree at least, familiar with the methods used and the problems under investigation in the other. No one will deny that many of the important discoveries of recent years were elaborated in the laboratory, but the ideas underlying many even of these were born in the clinic, and the laboratory results had to be further studied in the clinic before being successfully used with patients. Such work can be done most efficiently where there is a co-operative clinical-laboratory unit, rather than in a ward with indirect laboratory connection.

We may conclude, then, in general, that research in clinical medicine will be most productive when carried out on disease as it naturally occurs, that is, in the patient, by men who are fitted to study it from all angles by whatever means available, and that the clinic and laboratory where such investigations are conducted, should function, if possible, as one synergic unit. Many important indications as to the nature of disease and methods for investigating it will ever be furnished by bedside study; these will have their use in guiding, initiating and controlling the work of the laboratory, but the effectiveness of the relatively simple observational mode of approach alone is, in general, diminishing, because of the complexity of modern medicine.

The fact that this discussion is taking place suggests that we are not altogether satisfied with the present organization of clinical research. The reason, I think, is that there is not sufficient opportunity for the conduct of investigation in accordance with the principles just outlined. It is curious to reflect that the clinical study of disease, as it occurs in the sufferer, is less well organized and endowed in these islands, at least, *mutatis mutandis*, than is investigation in almost any other branch of science; this is all the more remarkable because disease is accountable for the greater part of the suffering and unhappiness of the human race. Moreover, it is well known that in communities where disease is being actively investigated by the synergic working of the clinic and laboratory, bedside observation is most careful and accurate, and therapeutic aid is, in general, most efficient, because of the stimulus of productive research on both teachers and practitioners.

The question we might now put to ourselves is: How are we to organize our clinical researches? If our public hospitals were acquired by some wealthy Crœsus, and if we were to be furnished in return with funds to build up and equip a new hospital organization, I think we should set about our task actuated by somewhat different principles from those that stimulated the comparatively haphazard growth of the present hospital organization. We should design our hospitals with four principles, at least, in view:—

(1) The efficient care of the sick.

(2) The study of disease, as it naturally occurs in patients, by all co-ordinated available means, that is, clinical and laboratory, observational, functional and experimental (by the latter I mean the formulation and testing of hypothesis), as well as from the minute examination of necropsy and biopsy material.

(3) The teaching and training of students, post-graduates, research workers and nurses.

(4) The institution of Hospital Social Service for after-care and after-study, as well as for sociological reasons.

As, however, such ideals are at present unattainable on a large scale in a world more or less impoverished, one can only keep them in mind in an endeavour partially to remedy an imperfect situation.

The time at our disposal is not sufficiently great to enable one to discuss the position exhaustively, but there is one aspect of it that should repay consideration; should our research workers be whole-time or part-time, and should the man in practice, with a sound hypothesis or a reasonable or tentative solution of a practical problem in disease, be afforded an opportunity for working out his idea?

There is much to be said in favour of the whole-time investigator in receipt of a salary sufficient to enable him to live in the degree of comfort adequate to his scientific and professional status, with reasonable security of tenure; he will be able to devote his whole time to his studies without the distractions of routine teaching, ordinary private practice, or consulting work; he will have leisure for thought, and

the circumstances under which he works will permit him to view his problems with a logical, critical, and scientific eye. His teaching should be confined mainly to demonstrations and lectures bearing on his own particular line of work. In order that he may not become too absorbed in his own comparatively restricted field, and, becoming narrowed in outlook, lose a balanced perspective on medicine as a whole, he should attend the staff meetings of the whole unit, so that he may learn as well as teach; he should keep in close touch with the learned medical societies, and maintain intercourse with outside teachers and practitioners. By such contacts he will foster broadmindedness in outlook as well as productivity in work, and his problems will be ventilated with reference to what Lewis calls curative medicine. Above all, he should guard against arrogance and preserve the spirit of scientific humility in his mental receptiveness. There is, no doubt, some danger—I have seen it happen—that the whole-time worker, if he omits such safeguards, will neglect the art of medicine for the science, will become disdainful of the psychological aids and kindnesses to patients (considering them wasteful of time and "unscientific") upon which their successful handling so much depends. The pendulum is now too far on the side of curative medicine—we must see to it that it does not, with the development of the whole-time investigator, swing too far to the scientific side and make the means the end; the investigator must keep in mind that the prevention and cure of disease is the objective to be reached and scientific accuracy the sign-post on the road. In many cases, it may be desirable that the full-time worker be an official of the University or Medical School, as well as of the hospital; this idea is in practice in many places in the United States. Finally, it may be said that such whole-time investigators (I am not speaking now of the whole-time professor or teacher who devotes a small part of his time to research) have contributed so much to progressive clinical medicine in recent years that their numbers and their facilities must increase rather than diminish.

The part-time worker cannot be said to be such a success. Admittedly, this statement is not universally true, but, on the whole, it is difficult to sustain interest in research and at the same time to have one's mind disturbed by the calls of practice; the psychological atmosphere of investigation is so different from that of practice that the mind does not usually give of its best to either when it is engaged with the problems of both. The only justification for the part-time worker in organized clinical research is either want of funds to equip and pay him for his full time, or, in certain cases, the advisability of giving a man in practice the opportunity to test a promising hypothesis. Undoubtedly, there are men in practice who have important ideas which they wish to elaborate, who are willing and able partially to sacrifice the rewards of practice therefor, and who are so mentally endowed that they can readily change from the psychological atmosphere of practice to that of research. Such men are not common, but those in authority should be able to recognize them and afford them the necessary opportunity for part-time clinical research. As an example of clinical research of the highest order, carried on for years in the course of a busy practice, one readily recalls the work of the late Sir James Mackenzie. It is not always that ability can conquer lack of opportunity as his did; we should see to it that opportunity is always present, otherwise some day we may fail to facilitate fruition of some important and far-reaching hypothesis.

It may not be always advisable, however, for the worker to make his inquiries in a research clinic. If his material can be assembled there, then, his studies being centralized and his equipment being at his hand, his efforts will probably be economical both in time and in money and his results more accurate. But such centralization is not always possible, because, for example, of symptomatological diversity, or chronicity, of the diseases under investigation. Then, he may be

compelled to do his work in the field or in the general hospitals. This, however, does not detract from the main thesis of this communication.

It is obvious, to be sure, that the clinical research worker must keep abreast of the literature of his subject and be prepared to test or apply in the wards any purely laboratory discoveries which may have a bearing on clinical medicine.

It would lead us too far afield to enter into a discussion of how the clinical research worker who takes investigation as a career should be trained. Suffice it to say that, having had a year or two of sound clinical experience and a period of general laboratory work, he should study, under direction, some comparatively simple clinical problems, doing both the bedside and laboratory work himself; the supervision of his early research should not be dictatorial but rather suggestive, and the exercise of his native logic should be unhampered; he should gain experience of experimental work with animals, so that he may later be prepared to use this method, whenever necessary, in his more advanced clinical investigations: then, when he undertakes subsequently more difficult clinical research, he will usually be in a position to acquire, devise, or advise upon such methods and technique as may be necessary for the elucidation of his problems. Sometimes complicated and intricate procedures are necessary for the solution of clinical questions, methods involving special knowledge of a particular branch of science, and too technical for the worker to master within a reasonable length of time—here co-operation with another investigator who possesses the requisite skill and judgment in the particular subject is frequently productive of success.

There is needed at present some organization to promote research in clinical medicine; some definite plan is advisable, rather than the pious hope that the goodwill of the leaders of our profession will stimulate a co-ordinated attack on the problems of disease. Why should there not be formed a Society of Hospital Teachers and Consultants, or even a Federation of Hospitals, for the advancement of research in clinical medicine? Such a body might be able to collect some funds and allocate them for organized research, and even might allocate the problems themselves, in order to avoid unnecessary duplication of effort and to ensure that work might be undertaken under favourable conditions. Scientific meetings of such a society might have an important influence on productivity.

It is, I think, generally true that a period of investigation makes one a better teacher and a better practitioner of medicine, because it makes one think of disease in terms of physiology. Why should the participation in a piece of research in a physiological laboratory, or in the wards, not count in addition to academic achievement, in the election to the junior hospital positions? Similarly further investigation might well be considered, amongst other things, as a desideratum in the appointments to the senior staff. Of course, this system should be confined within the bounds of reason, because of the double nature of our work, namely, the science and the art of medicine.

If some full-time research positions, tenable for a limited period of years, say five, were established in our hospitals, they should form a good recruiting ground for at least some of the higher clinical teaching positions. This would also mean that because a man had once joined the ranks of the researchers he need not be compelled to remain there always—the advisability of providing a method of escape from work that might eventually prove uncongenial or unfruitful is obvious enough. And there can be little doubt that a period spent in investigating little-understood fields in disease would enhance rather than diminish ability to diagnose and treat disease.

We should keep clearly in mind that however research in clinical medicine is conducted, and however noteworthy are its results, the final tests of reliability must be made in the clinic and in the practice of medicine outside its walls. For us,

successful investigations which do not lead to results applicable to disease in man are either of academic interest or the starting-point of further researches. Moreover, we must not lose sight of the important fact that the clinical study of disease, as it actually occurs in patients, will not only suggest problems and initiate attempts at their solution, but can often furnish guidance and give directional indications of great importance to the co-operative laboratory investigations, which may make all the difference between partial and complete success.

To summarize, then, we may say that organized research in clinical medicine should be carried out, whenever possible, in a special department of the hospital or in a clinic specially designed for that purpose. This department or clinic should be well equipped with all the necessary laboratory and library facilities and staffed by individuals who, in general, devote their whole time to clinical investigation, their teaching being comparatively limited and specialized. The laboratories and wards should act as a unit for the purposes of research, the workers for the greater part being familiar with the methods of both bedside and laboratory. It must be recognized, however, that in clinical medicine there frequently become manifest problems the study of which may be impossible in a clinical-laboratory unit; in such cases the research necessary may have to be undertaken in the field, by the observational or experimental method, or by both; it is here that discretion and understanding on the part of those in authority are especially needed, not alone in the organization of the work, but in the choosing of suitable workers and in providing opportunity, equipment and material. Such concepts as these should not interfere with the provision of aid to men in practice who have the requisite qualities, opportunity and ideas for carrying out investigation in disease problems.

If there is one lesson that can be learned from the material aspect of the age we live in, it is that *research pays*. In clinical research the return will be better medicine, greater and more prompt relief of suffering, improved teaching, diminished mortality-rates and increased longevity, not to speak of the increased confidence and satisfaction which will accrue to the whole medical profession from work well done.

Dr. Helen Mackay: A month or two ago I heard the opinion of an American professor of pædiatrics on recent clinical research in this country. It was scarcely flattering: "You are doing practically none," he said. "Research by pure laboratory workers—yes, certainly; but there is practically no clinical research coming from the British Isles." Like other sweeping statements, this is obviously incorrect as it stands. We all know of new contributions to knowledge coming year by year from bedside workers in this country; but that any such statement should be possible points to a state of affairs badly in need of alteration,

We have no reason to suppose that as a people we lack our fair share of workers with the brains and character to carry out clinical research; our records in the advancement of knowledge during the last centuries and in scientific research to-day certainly do not support any such view. Why then are we doing no more in the special field of clinical research? I think I am expressing the views of many when I state that this is due to lack of facilities, and this in its turn is due to the fact that our country now lags far behind others in the recognition of the value of clinical research, and consequently in the encouragement given to the clinical investigator. That, in spite of all their handicaps, clinicians in this country are, year by year, advancing the science of medicine is but an indication of the talent that awaits better opportunities. Much of the clinical research now done in England is undertaken under heavy disabilities by doctors who not only have to

contend with inadequate facilities, but must do so with the energy left over after earning their livelihood in other ways.

Surgeon Captain Dudley, in his paper read before the United Services Section last week, holds that the Services offer an ideal field for clinical investigation. I must confine myself to the civil field as I know nothing of the naval and military.

Let us consider the primary needs of the clinical investigator. These are: adequate clinical material, the sympathy and assistance of his fellows, and, above all, time—with its inevitable corollary money—for reading, for thinking, as well as for the collection and correlation of facts. I propose to take these points in order, and will endeavour to suggest some ways in which clinical workers might be given better opportunities than exist to-day.

Most investigators, whether they rely primarily on the observational or primarily on the experimental methods which have been discussed, find that they need to obtain their human material in a hospital or other institution. General practitioners, no doubt, have plenty of material, but—as they are the first to admit, often with real regret—under conditions which render properly controlled investigation all but impossible to most men; that shining exception, Sir James Mackenzie, cannot be held to show that general practice offers an easy or hopeful field for research. Moreover, the investigator must have *control* of his material, in other words, he must have medical charge of hospital beds, or of out-patients, or of an institution, as the case may be. If he has not complete charge he is dependent on the good graces, the sympathy and understanding of those who have, and complete co-operation under such circumstances is not easy to achieve. We all know instances where a laborious investigation has been rendered useless by an unwitting change in some detail of treatment made, in the absence of the unfortunate investigator, by a member of the honorary staff of the hospital. Hence we may say that the clinical research worker needs, as early in his career as may be, a hospital appointment where he has charge of beds and out-patients, and this, with our present system of voluntary hospitals, means that he must have the post-graduate experience, standing, and qualifications rightly demanded for such an appointment. Clinical material is certainly available in hospitals other than the voluntary ones, and in the future let us hope that these institutions may contribute largely to the advancement of knowledge, but in the past one cannot say that research has been encouraged in many of them. Some years ago at dinner one evening, four or five medical members of a service which shall be nameless, but which was incidentally paid for out of public funds, were discussing the probable allocation of certain senior appointments then falling vacant, and I learned with interest that it was unanimously agreed that if a man had pressed for improvements, for fresh facilities, or for more modern technical appliances, he had injured his prospects by such unpopular proceedings, whereas men who led a quiet life and left things as they found them, causing no trouble, would certainly be preferred over him. Can one wonder that little clinical research has come out of these hospitals?

This brings me to the second need of the clinical investigator, namely, the sympathy and assistance of his fellows, not only that of his medical colleagues, on whose goodwill he is dependent in so many ways—whose help is generally fully and freely given—but also of the nursing staff and of the lay management of the institution. I should like here to say how much I personally owe to the generous help I have so freely received at the hands of my colleagues, and of members of the nursing profession, and how fortunate I have been in the opportunities that have fallen to my share. Nurses, as we all know, are often already working at full pressure, and yet any investigation will almost certainly entail extra work for them.

Nevertheless, most of us have learned to count on their assistance to the maximum of their powers in spite of their already very heavy work. Yet it is not fair to overtax such willing workers, and our hospitals are obviously not arranged to provide that extra nursing or other assistance that would often be of great value. As regards lay opinion, some of our hospital boards of management recognize the value of research, but the complete ignorance, and hence the want of sympathy, of many of the lay public with regard of all matters pertaining to medical research, results not only in lack of encouragement, but sometimes in direct obstacles being placed in the way. I cannot help thinking that if some of our newspapers would make an effort to educate public opinion in this respect much good might result. As an instance of the hindrances that arise from lack of comprehension, I should like to quote the following example which has come to my knowledge during the last few years. A piece of investigation, planned to last about twelve months, was undertaken at a certain institution with the consent of the lay board of management. When little more than half the year had passed, the authorities, probably as the result of changes in personnel, suddenly requested that the work be closed down within the next fortnight as "the institution was not intended for research." Fortunately, when it was explained that the whole of the work up to date would be thrown away, the lay management agreed to a few months' extension. That place is now closed to research, whereas under proper management, the material offered a field for very useful work.

And now I come to the crux of the matter. All clinical research must make large demands on the time, the energy, and the thought of the worker. This is true whether he collects his facts by the method of observation or by that of experiment, or by both methods. No one can give the time unless he is also provided with the means of existence; few will give it if they believe that by doing so they will condemn themselves to an income absolutely disproportionate to that earned by their colleagues in every other branch of medicine. What then are the prospects under present conditions for the young medical man without private means, who is meditating whether he will turn his energies to clinical research? He may, of course, decide to earn his livelihood in other branches of medicine and devote his leisure to research, but the energy and time thus left over are not likely to be large. If his aim is consultant work or general practice he in no way enhances his prospects, but possibly the reverse, by turning aside temporarily to clinical research. Moreover, he will certainly suffer from "that most distracting of thoughts," as Sir Thomas Lewis has called it, "the immanence of an alternative career." With luck the young graduate can obtain a research scholarship varying in value from, say, £50 part time to £350 per annum full time, non-resident, and lasting from one to three years; the more valuable of such scholarships usually go to men or women who have had a number of years of post-graduate experience and who may already have held important posts such as university lectureships. Contrast this remuneration and the qualifications required with the salary of £600 a year as a minimum for which the profession has successfully fought in the public health services. When the first scholarship has come to an end, the worker, if he is lucky, may obtain another scholarship, or research grant, but at the best these are only temporary and hold out no prospect of security of tenure—the grants given by the Medical Research Council are all, I understand, yearly awards. If a man is fitted for research, it is unlikely that his earliest efforts will be his best, for, as in other branches of medicine, he should profit by increasing experience. To begin to train men for research and give them no stable appointment is surely a waste both of men and money. The small earnings of earlier years would not matter if the prospects for later years were more encouraging, but there is at the present time unfortunately, no prospect of any stable position for the man who devotes himself to clinical research. The Medical Research Council, in their last annual report, have

said with truth that "there can never be a successful . . . recruitment of young men of ability for clinical research until there are at least a few stable positions in sight, the occupation of which at middle age will provide reasonable remuneration." Further, this report states that "a very small part (of the research work supported by the Council by annual grants) has been done by men engaged in clinical work and studying disease as it actually presents itself in human beings," and small cause for wonder, under existing conditions! There are, of course, in this country at some of the teaching hospitals, medical units whose heads hold permanent clinical appointments, but I understand that, as at present arranged, the demands made by teaching are so great that these posts cannot be said to offer either satisfactory opportunities for research or for training others in the methods of research.

Contrast these conditions with those obtaining in other countries. Professor Moore has told us something of the facilities existing in American hospitals. No doubt many of those present know more than I do regarding conditions in Germany and Austria, but I understand that in those countries at every university hospital up and down the country, and they have many more small universities than we have, research is considered an integral part of the work of the institution and is made possible by the salaried clinical appointments offered by these hospitals. A University Kinderklinik at which I had the privilege of working was staffed by two professors and five or six *Dozents* and *Assistents*, the latter all full-time men of high professional standing, of the type aiming at professorial chairs. These men direct the activities of the recently qualified graduates who assist in the general routine work. I hope no one will think that I am asserting any general superiority of the German system over our own, for I do not know enough about it to be able to make a fair comparison, whereas I do know the remarkably valuable experience given to large numbers of young graduates by our own system of short-time resident hospital appointments. Yet in this particular, in the opportunity offered by the German hospitals to the clinical research worker, there can I think be no question that they are far ahead of us. Last month I had the pleasure of visiting the University Kinderklinik in Freiburg-im-Breisgau, a town of 100,000 inhabitants, about the size of Reading. It is under the charge of Professor Noeggerath, as no doubt many of you know, and I was told of three or four separate pieces of clinical research then in progress, the work being combined with animal experiments under the same roof. Not only is the hospital well equipped as regards all the ordinary special departments and laboratories, but they have also, I understand, a room specially fitted for metabolic work. In addition they have an excellent library provided with the current periodicals, as a good library is recognized to be an essential need of a research worker. And this was the Department for Children's Diseases alone, of the Freiburg Medical Faculty. How many children's hospitals in London, we may ask, have a library of even 100 volumes, not to speak of foreign journals? There is certainly no town in England of similar size that could show such a children's hospital. My knowledge is chiefly confined to children's hospitals, but I understand that the conditions are the same for general and other special hospitals.

In the hope of arousing further discussion I will sketch the type of appointment that I should like to see created in the field of research. The first scholarship, given for a period of two or three years, should serve to give a man or woman an initial training in this field and would provide some indication of his fitness for the work and of the appeal the work held for him. For those who desire to continue in this branch of medicine I should like to see open advertised appointments offering some security of tenure, possibly after a certain probationary period, together with the prospect of financial advancement. It may be argued that such posts would be abused, or that they would be filled with those whom we may for the sake of brevity characterize as "duds," but I see no more reason why this should happen with clinical appointments than with

the laboratory research appointments which now exist—any safeguards necessary in the one case would probably meet the other. There are certain arguments in favour of attaching such posts to specified institutions, for example teaching hospitals, but the widest field would be obtained if restrictions were reduced to a minimum, and I hold that the primary consideration should be to appoint the right men or women and give them the greatest possible measure of freedom. A young graduate might begin his career in research at a small hospital and later become a member of the staff of a teaching hospital, and he could carry his research appointment with him from one institution to the other. On the other hand, public-spirited persons wishing to help a particular hospital by their benefactions, might well consider that an endowment for the post of "research physician" or, better still, a "research unit," would be an excellent means of enhancing its usefulness and good name.

Whether the research appointments should be full term would, I think, depend on circumstances. One man might most successfully combine with his research teaching or paid routine work of one type or another; another would do his best work with a full-time research appointment; both types should, I think, exist. More senior members of this clinical research service might be given the privilege of recommending candidates for appointment to temporary junior research posts in their own institutions; such an arrangement should be a valuable means both of finding talent among the young graduates of a teaching school and of utilizing to the full the stimulus of an inspiring investigator.

All this at present is a dream, but when our profession and the public at large wake up to the urgent need of clinical research, it is a dream which might rapidly be converted into reality to the great and lasting benefit of the community, and incidentally the enhancement of our professional credit abroad.

Lord Riddell said that in this, as in other matters, the question of money was the difficulty. The taxpayer and ratepayer were heavily oppressed already, and would rather run the risk of a little extra ignorance as to the cause and cure of disease than pay higher rates and taxes which might themselves cause disease. What struck the layman was the lack of knowledge concerning common troubles, such as colds, rheumatism, tonsils and adenoids, pyorrhœa and so on. He (the speaker) resented the suggestion that the most valuable discoveries were made abroad. He thought that if a list could be compiled of the important discoveries made during the last fifty or sixty years, Britain would come well out of the investigation. Compared with other nations we were bad advertisers. We had the further defect that a hypersensitive section of the community were always belittling their own country.

Dr. F. Parkes Weber said that some evidence against the popularity of research amongst doctors themselves was afforded by the extraordinary number of modern general medical and surgical textbooks in existence. Physicians and surgeons seemed to vie one with another in bringing out general textbooks, the making and compiling of which must consume endless time and trouble, whereas it was rather the writing of monographs that fostered the spirit of research. He thought that under the heading, "Research in Clinical Medicine" should be included the doings of workers in macroscopic and microscopic pathology, and much work done in clinical laboratories just as that done in the wards. The physician could go into the laboratories and the histologist into the wards to see the lesions and tumours, on the "biopsy" findings in which he had afterwards to report. Moreover, when a biopsy examination revealed very unusual or unexplained

microscopic features, there seemed to be no very large classified storehouse of microscopic sections where exhaustive comparison could be made.[1]

Dr. Albert Eidinow: I have listened to the openers' papers with much interest but with some disappointment, for I had wished to hear something which would be of help in giving medical research its proper status.

A clearer definition of the words "medical research" is needed. If this research is defined as pure original discovery, then this should be open to every physician who was capable of investigating discoveries in medicine. Adequate facilities should be freely given to any such medical practitioner.

It is, however, known from the study of the research work done in the past, that the majority of it, over 90% even, is not original research but a series of scientific investigations, and much of the clinical research in medicine falls under a similar category. From the practical point of view it must be realized that this type of investigation can be readily carried out by trained scientists who really need no medical qualifications but are trained as biochemists, bacteriologists, etc. Such full-time workers have efficiently carried out numerous scientific investigations and have served much useful purpose, but these investigations are not true medical research. The young physician who has just completed his training at hospital is an amateur in the technique of research and, as a result, his training originates from making stereotyped examinations and tests. He is doing scientific investigation.

Another problem which needs solution is that of the work done in connection with the standardization of drugs and sera and other therapeutic agents. In the past this has been carried out in research laboratories by adequately trained and skilled workers. Although this work is one of the greatest importance, it is doubtful if it should be done in research laboratories and with facilities which were intended and endowed for medical research. The problem can be summarized as a distinction between (1) original discovery, which is true medical research, (2) scientific investigation, which needs highly skilled and trained men, quite apart from their capabilities and work as physicians, and (3) the problem of standardization.

Finally, speaking from the physician's point of view; I urge that some definite scheme is necessary to give facilities to original discovery, and this should be open to any clinicians and others who are suitably qualified and who are gifted with inspiration.

Dr. Leonard Findlay said it was natural that we should be anxious to increase the growth of our knowledge, but he was not sure that the methods suggested by the openers of this discussion would have that effect. Certain general considerations must be borne in mind. He did not believe that the observational method in medicine was exhausted, but one could only wait for the man with the eyes to see. Even in his own student days, physicians still lifted the blankets from hemiplegics and patients who had disseminated sclerosis, without seeing that the great toe was kept hyperextended or that when the soles of the feet were stroked the plantar reflex was in any way abnormal. It was only when Babinski, with the eye to see, came along, that attention was drawn to the fact, and to-day there were no doubt many such phenomena waiting to be observed.

We should be careful about drawing a dividing line between the ward and the laboratory. He wondered how the stethoscope was looked upon on its introduction

[1] In regard to *macroscopic* research it may be noted that in spite of our many medical libraries there exists no atlas (corpus) of pictures and diagrams of all known types and varieties of congenital-developmental diseases of the anatomical (macroscopic) "mutation" class. Therefore, it is often impossible to find out whether the special features of a case that turns up have yet been described and investigated.—[F.P.W.]

and how the method of urinary examination was at first regarded. The fact that urinary examination to-day might be complicated and was carried out in the laboratory rather than at the bedside, was no reason for considering such methods outside the province of the general physician. Every new technique or instrument of precision opened up new fields, and the lecture delivered to the Society by Chevalier Jackson a fortnight previously was a brilliant example of the way in which the boundaries of clinical investigation were extended.

He had a difficulty in accepting the doctrine of two types of physicians—the clinical or practising physician and the research physician—as promulgated by Sir Thomas Lewis and repeated this afternoon. There was only one type of true physician, at least so far as the members of our general hospitals and teachers of medicine were concerned. The greatest function of a teacher was to inspire his pupils, and he alone could do this who was an active worker and was attempting to unravel some of the many problems as yet unsolved.

Finally, there was much talk of rendering the research worker independent, in the hope that he would do better work. Did history lend any support to that idea? It was the inward urge that was required, and this could not be made though, of course, it could be encouraged. Much of the great work of the past—artistic, literary and scientific—had been done by sick and poor men. He questioned if the necessity of earning a livelihood had hindered the right man from doing what he was most interested in doing. Jenner and Lister were both practising doctors, and John Hunter, who put in more research work than probably any other man in the field of medicine, was always cursing the time he had to steal from his dissecting room in order to earn a "damned guinea."

Dr. G. W. Theobald said that it was necessary to decide whether research in clinical medicine was desired in this country—for research almost invariably meant more pricks for the patient. If research was earnestly desired, the hospital system in England would have to be fundamentally changed. It was ludicrous to think that young men on the staffs of three or four hospitals—separated by long distances—could conduct serious investigations. He believed that the inevitable corollary to success in practice was failure in research.

Dr. J. Kingston Barton said he called to mind an American professor of medicine advising a large class of qualified young doctors leaving for a post-graduate visit to Europe, that after first visiting Vienna, Berlin and Paris, they should save time to spend some weeks in Great Britain where they would learn how to be really good "doctors." A compliment to our clinical teaching!

Looking back on the sixty years that had passed since he entered St. Bartholomew's Hospital, he could only express his intense admiration for the steady and great progress, culminating in the present excellent clinical units; similar advances were seen at every other London hospital with medical schools attached. In his (the speaker's) opinion it seemed far wiser to change the special research staff every five years, than to appoint whole-time permanent research workers.

Dr. W. R. F. Collis said that he spoke with some feeling, as one who was actually engaged at the moment in clinical research. Professor Findlay was right when he said that research should not be made too easy for young men, for if too many easy jobs were provided, many unsuitable individuals—those who found other branches of the profession too strenuous—would flock into these posts, but what was needed was a future in clinical research for the young man who won his spurs.

At present, after a time, every one engaged in clinical research came to certain cross-roads and had to make up his mind whether to get into practice or get into debt.

He found at present a definite antagonism between the clinician and the laboratory worker with contempt for the other on both sides. So marked indeed was this that if he (the speaker) worked for any length of time in a laboratory he was dubbed a "lab worker" by the pure clinicians and thereafter held to be incapable of clinical responsibility, or, if he went into the out-patient department to see clinical material, he was looked at askance by the laboratory workers.

In future, if this country was to hold its own in clinical medicine, it would be necessary for the physician to have both a clinical and laboratory training.

Section of Ophthalmology.

[*October* 10, 1930, *continued.*]

Calcareous Keratitis.—ADRIAN CADDY.

Patient, a woman, aged 63, has been attending the Royal Westminster Ophthalmic Hospital. Four months ago a nodule developed at the limbus on the inner side of the right eye, and there is now a semilunar mass of infiltration extending half across the cornea, with vessels coming in from the sclerotic, but without any acute inflammatory change. There has been no corneal ulceration, and there has never been a sign of any breach of surface. The Wassermann reaction was negative, and examination of the fundus shows no abnormality.

The treatment has been chiefly symptomatic; she has been treated by iodides and atropine, and by the application of diathermy. We have also tried injections of tuberculin. The condition seems to be of the nature of a calcareous degeneration with a slowly advancing edge, shaped like a new moon, which has attacked half the cornea.

Traumatic Zonular Cataract.—FRANK W. LAW, F.R.C.S.

I. G., a girl, aged 14, has complained of defective vision of the left eye for two years. Gives a history of having had a blow in the left eye from a twig four years ago. No history of other eye trouble, or of fits, rickets, measles or pertussis. One of a family of nine; all the others have normal eyes.

On examination.—Right eye: Emmetropic, and otherwise normal, except for some well-marked vitreous bands; I am not prepared to say whether these are pathological or not. Vision $\frac{6}{5}$. Left eye: The lens, which I think is dislocated, shows a zonular opacity. The cortex overlying the zonule is clear except below, where there is also a patch of iris pigment on the lens; this would I think indicate that this is the point of trauma. Peripherally the cortex is clear; centrally there is what would be, except for the presence of minute spicules of opacity, an optically empty interval. Vision $< \frac{6}{60}$.

A diligent search for notes of a similar case has, so far, met with no success; I assume, therefore, that the condition is a rare one. There is a resemblance to a "congenital" lamellar cataract, but I would adduce the following reasons against that diagnosis: (1) it is monocular; (2) it was noticed first when the patient was aged 10; (3) the general medical history is against it; (4) there are no "riders"; (5) there is a complete absence of the regular pattern typical of a lamellar cataract; (6) the edge is irregular.

I discovered the case when working in Mr. Davenport's clinic at Moorfields, and I am indebted to him for permission to report the case.

Pseudo-Coloboma of Iris.—FRANK W. LAW, F.R.C.S.

K. S., a boy aged 12, gives a history of always having had a black spot in the eye. There are no subjective symptoms, and vision in each eye, with a weak myopic correction, is normal.

The right eye shows a local absence of iris stroma on the nasal side of the iris. The underlying pigment layer is complete, and there is no apparent lack of iris musculature. The stroma is absent peripherally as far as the "collarette"; at one point the coloboma transgresses this line, a bridge of stroma being stretched across the pigment layer. Development has evidently proceeded normally as far as the neural ectoderm is concerned, but there is a local failure of paraxial mesoderm.

The interest in the case lies in the speculation as to whether the coloboma is due to: (1) failure of the ectoderm, in its growth, to draw forward the mesodermal layers, or (2) excessive atrophy of the mesodermal iris, which originally stretches well over the definitive pupil, past the pupillary area, and back to the "collarette."

Retinal Pigmentation.—FRANK W. LAW, F.R.C.S.

R. Y., a boy, aged 5, came to my clinic as a refraction case. His corrected vision is apparently excellent in each eye. I have examined both his parents and his brothers; all have normal fundi.

Present condition.—Both fundi show scattered guttate and araneiform patches of pigment, very fine in nature, all over the retina. If this is a case of retinitis pigmentosa the condition is unlike any that I have seen before under that heading.

Early Diabetic Retinitis.—J. H. DOGGART, F.R.C.S.

Patient, a woman, aged 47, has had diabetes for more than two years. In April, 1930 left-sided herpes ophthalmicus developed, complicated by iritis. She attended the London Hospital two weeks after the beginning of the attack; the fundi were then normal. She has been using atropine in the left eye ever since. She thinks that her sight has been growing worse during the last few weeks. Scars of the herpes attack can be seen on the left side of the forehead and on the left eyebrow; in the left eye are shrunken keratitis punctata spots and deposits of pigment on the anterior lens capsule. There is also coronary cataract in each eye. The fundi are arterio-sclerotic, and show at each macula multiple minute exudates and punctate hæmorrhages. Similar hæmorrhages can also be seen far into the periphery, especially in the right eye.

The case is one of diabetic retinitis in an earlier stage than is usually seen among persons who come to ophthalmic out-patient departments.

Corrected vision in the right and left eyes is $\frac{6}{9}$ and $\frac{6}{12}$ respectively.

I am indebted to Mr. Goulden for permission to show the case.

The PRESIDENT said that there was always disease of the blood-vessels in cases of retinitis. In cases of severe diabetes, even to-day, in spite of treatment by insulin and of the disappearance of the glycosuria, the retinal changes remained. The reason for that was probably that the minute blood-vessels were seriously damaged by the disease.

Multiple Foreign Bodies in the Corneæ.—J. H. DOGGART.

The patient, a woman, aged 27, came to the Royal London Ophthalmic Hospital in July, 1930, stating that for the previous two years her eyes had been occasionally misty; and had been irritable for the last six months. She was employed in a firework factory making crackers, and every now and then some of the powder exploded in her face. In the cornea I saw a number of minute foreign bodies, some whitish, some brownish, embedded in the epithelium and in the anterior layers of the substantia propria. The best vision in each eye was $\frac{6}{18}$. With the slit-lamp the posterior band of each cornea was abnormally accentuated and was of a bluish tinge. I saw the patient again in October and the eyes were then less irritable. She had become tolerant to the presence of these multiple foreign bodies. The same tolerance was acquired by a man aged 24 whom I saw recently. His eyes are much better now, unless he drives a car more than 150 miles in a day. His corrected vision is $\frac{6}{6}$ in each eye.

Perhaps someone with a knowledge of chemistry can say of what the particles in the present case consist. I think the powder with which these crackers are made consists of nitre, charcoal and sulphur; sometimes lead nitrate, or barium nitrate. I am indebted to Sir John Parsons for permission to show this case.

Mr. T. HARRISON BUTLER said that many of these crackers were made in Palestine, and were let off in public at the Feast of Ramadan; consequently many cases of this kind were seen at the hospitals there. The yellow particles were, he believed, realgar, (disulphide of arsenic), which when mixed with chlorate of potash formed a mixture which detonated on percussion or friction.

Case of Rodent Ulcer extending into the Orbit.—EUGENE WOLFF, F.R.C.S.

This patient, aged 64, was first seen at University College Hospital in June, 1928; he then had a rodent ulcer near the inner canthus of the right eye. It was treated with surface applications of radium for four months. The skin healed, but the growth involved the conjunctiva and then extended back into the orbit. I excised the growth extensively, but after a few months it recurred. In July, 1929, needles each containing 4 mgm. of radium were inserted into the growth, three to a depth of 1 cm., a fourth being put in deeply along the lateral wall of the ethmoid. Now, fifteen months after the insertion of the radium, there seems to be complete freedom from growth. It was usually said that, once a rodent ulcer had involved the conjunctiva, hopes of saving the eye were very small, yet this patient seems to have been cured, the eye and its movements being unaffected. In cases which involve the inner canthus it is important to put the platinum needle containing the radium along the ethmoid, as rodent ulcer in this region tends to extend back along the ethmoidal air cells.

My thanks are due to Sir John Parsons for permission to show the case and to Mr. Fatti, Acting Harker-Smith Registrar, for help with the insertion of the radium.

Discussion.—The PRESIDENT said that a mistake which he had once made might be a warning to Members to keep any case of rodent ulcer in which the growth was not too large for surgical treatment, under their own observation. He had once sent such a case from the hospital to a Radium Department. There was a small growth on the lid, and it could have been removed surgically. He did not see the patient again for eighteen months, and then all the lower lid had gone, as well as the conjunctiva, and the orbit had to be exenterated. The patient had been told, month after month during his attendance, that the condition was improving. In some cases radium seemed to act like a charm, but in others it did no good.

Mr. T. HARRISON BUTLER said that he had sent to a Radium Department a case in which the growth was chiefly confined to the conjunctiva of the lower lid. The patient had one application of radium, and was completely cured.

Massive Exudate.—J. F. CUNNINGHAM, F.R.C.S.

The patient, a girl, aged 19, has attended my Out-patient Department at the Central London Ophthalmic Hospital since June, 1930. In the left eye there is a large slaty-grey mass, which I think is an exudate. Since she has been under observation the outer edge has become crenated, and one or two bright spots have appeared, which I take to be cholesterin bodies. The swelling has not increased.

The PRESIDENT said he thought that the condition was the result of an acute patch of choroiditis six or more months ago, which was now subsiding so that tissue was forming. He did not think there was anything beyond an inflammatory mass.

Contact Glass for High Astigmatism.—J. H. BEAUMONT, M.B., Ch.B.

L. T., male, aged 42, salesman. This man was injured in a molten metal accident in 1912. Owing to failing sight he had to give up work ten years ago. The right eye shows extensive lens changes with much thickening of the anterior lens capsule, but the cataract is not mature. Right vision: $\frac{6}{18}$ not improved and J.12 with difficulty. The left eye has a corneal opacity covering the nasal half of the pupil. There is a pseudopterygium and there are two strands of adhesion of the

lower lid to the globe. There is trichiasis of the upper lid. Left vision is reduced to counting fingers; not improved by a mydriatic. The retinoscopy of the left eye is

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and, with two crossed cylinders + 8 D. cyl. at 10° and − 10·5 D. cyl. at 100°; the left vision is brought up to $\frac{6}{6}$ (4) and J.1. I have had glasses made according to this prescription. I thought of having two cylindrical lenses, flat on one side with a stenopeic slit between, but this would reduce the field of vision. With a contact glass, 9 mm. corneal curve and 12 mm. scleral curve, he now reads $\frac{6}{6}$ (1) and J.4 comfortably with a +7 D. sph. Sir Richard Cruise, to whom I am indebted for permission to publish this case, found no astigmatism demonstrable with the ophthalmometer. The patient has now been wearing the contact glass five hours, which is rather a long time for the first day.

Section of Psychiatry.

President—Dr. S. A. KINNIER WILSON, M.D.

[*November* 11, 1930.]

PRESIDENT'S ADDRESS.

The Approach to the Study of Hysteria.

By S. A. KINNIER WILSON, M.D.

THE vicissitudes undergone by hysteria in the succession of the centuries have varied prodigiously, and he would be a bold clinician who to-day would announce their definitive end. Phases of medical doctrine run their course and have their day, but hysteria goes on. Doubtless in the present era of psychological grace we who have been conscious of the immense strides taken by psycho-pathological research are prone to believe, if not, perhaps, to feel entirely sure, that hysteria has at length yielded its secret—a discovery often yielded before, but never, we fain would pride ourselves, with so valid a pathogenesis on which to base the claim. If, for the nonce, however, we approach the question from the standpoint of pure empiricism, confidence may conceivably be somewhat shaken.

To this empirical approach objection cannot be raised. No reason exists why study of the objective clinical phenomena of the condition should not be prosecuted, deductions therefrom as to their nature drawn, and generalizations of a nosological character formulated, or, at least, attempted. Nothing, however, has been more typical of this period of psychological study, so far as hysteria is concerned, than the comparative absence of research of an objective and empirical kind. Can it be that acceptance of the former method dispenses with all necessity to conduct the latter? If this be the case, then psychological theory stands to lose in impressiveness. It is not so very long ago since a distinguished protagonist of new conceptions of hysteria, in a psychiatry club of which I was a member, listened with mild impatience to my exposition of certain neuro-physiological peculiarities in hysterical symptoms, and closed discussion by declaring that since the neurosis had its demonstrable origin in a vita sexualis which did not run smooth its semeiology was of merely secondary interest and minor importance.

Possibly the outstanding feature of hysteria as revealed to us by the records of former generations and the knowledge of our own is the changes which its clinical syndromes have suffered. This simple fact of observation must appear deeply significant, as fruitful for theory as it is true in substance. The mediæval ecstatic, simulating in hands and feet the nail-prints of her Redeemer, is long since démodée, as is her eighteenth-century sister, melodramatically counterfeiting the emotional transports of a popular actress. I quote from Kay's *Portraits*, published in 1837:—

> At the first visit of the great Mrs. Siddons to Edinburgh, many were the fainting and hysterical fits among the fairer portion of the audience. Indeed, they were so common that to be supposed to have escaped might almost have argued a want of proper feeling. One night when the house had been thrown into confusion by repeated scenes of this kind, and when Mr. Wood (a popular surgeon) was most reluctantly getting from the pit (the favourite resort of all the theatrical critics of that day) to attend some fashionable female, a friend said to him in passing, "This is glorious acting, Sandy," alluding to Mrs. Siddons; to which Mr. Wood answered, "Yes, and a damned deal o't, too," looking round at the fainting and screaming ladies in the boxes.

What impresses in this echo from an unimaginable past is the insight displayed by the common-sense surgeon of that day. But let us come a little nearer our own time. The quotation is from a lecture on hysteria delivered at St. Bartholomew's

Hospital in 1866, by Mr. F. C. Skey, F.R.S., a then celebrated member of its consulting staff:—

> Thirty or forty years since . . . and for how many years anterior I know not, all the seaside towns were crowded with young ladies between 17 and 25 years of age and beyond it, who were confined to the horizontal posture, and wheeled about on the shore in bath chairs, on the supposition that they were the subjects of spinal disease. They were placed under much medical and dietetic discipline . . . and the large majority carried a pair of handsome issues in the back! Brighton, Worthing, Hastings, and other places on the South Coast were largely tenanted by these unfortunate females, to which a moderate sprinkling of young gentlemen was attached. What has become of all these cases? They appear to have vanished just in proportion as the eyes of the surgeon have been opened to the absurdity of inferring that pain alone, which locates itself with remarkable precision in hysteria on a given vertebra, can indicate the presence of organic disease of the body of the bone without collateral evidence in its favour.

No longer do the "circus horses" of the Salpêtrière perform before distinguished visitors as in the palmy days of Charcot; no more does their contorted musculature respond to the application of divers metallic rods, as Gilles de la Tourette was wont to demonstrate; seldom indeed is the clinician witness to the elaborate and protracted hysterical fits whose theatrical features were drawn with artistic skill by Paul Richer. The intimate correspondence of the historical phases of hysteria with contemporary medical predilections is responsible for the alternate tragedies and comedies of its treatment, and Morestin's remark embodies a shrewd estimate of the situation: "Les hystériques suivent à leur manière le mouvement scientifique, et s'adaptent au progrès de la médecine." Since the day (and long before it) of the insensitive and bloodless marks that stamped the witch as Satan's own the poor hysteric has done her best, has never failed to respond to the calls made on her. But to-day we seek the clue to the ailment in the unseen psyche, and she is somewhat at a loss accordingly; her elaborated somatic manifestations are rather at a discount. A cold scientific environment besets her, instead of a world of emotional extravagance and limitless credulity. So a defence-hysteria is now more à la mode, no less egocentric if more utilitarian; with an eye to the main chance, the hysteric turns to the possibility of compensation for trauma, or seeks to escape from unpleasant reality by a flight into neurosis—at least, so we are assured. The times have changed, and we, both physicians and hysterics, have changed with them.

Yet, when all this is said, it remains true in a deeper sense that if hysterical fashions vary, their kaleidoscopic patterns are composed of unaltering, instinctive and impulsive reactions; thus can its clinical characters be recognized on the Greek vase depicting the ecstasies of the frenzied mænad, in the records of some New Testament miracles, in mediæval paintings of demoniac exorcism, in modern accounts of camp-meetings, spiritualistic séances and religious revivals, of disease-mimicry in school-girls and shell-shock amid twentieth-century warfare. Beneath surface diversities the essence of the phenomena involved has not been modified. And further, where old beliefs linger in the public mind, where superstition is rife and mysticism rampant, there still is to be found the favourable and appropriate milieu for hysterical exhibitions of antiquated form and guise even in this epoch of scientific enlightenment. The literature of demoniacal possession, recently collated and analysed by Oesterreich, contains not a few references of an authentic kind belonging to the last two decades only. Nor, in the nature of things, is it likely that such hysterical traits and expressions will really disappear; human culture may progress, but a Messina earthquake or a world war will lay bare hidden reactions among some of the species, at all events. Leprosy, rabies and malaria are ancient diseases, but epilepsy and hysteria are older still: are they as old as human nature itself? Their antiquity and ubiquity might almost suggest this; and since epilepsy is scarcely anything else than a physiological

reaction, which anyone soever will exhibit provided he is injected with a convulsant, it becomes curiously interesting to discuss whether hysteria, too, is but a name for a reaction, capable of being exprcssed in dynamic, neuro-physiological terms.

It is nearly twenty years since I wrote a paper in *Brain* on this subject, in which certain ideas respecting the objective study of hysterical phenomena were outlined.

A brief quotation will indicate what is intended :—

> I have repeatedly said that I believe we must depend on the objective signs of hysterical disease if we are to progress towards its unification. Janet himself holds that the intrinsic examination of cases of hysteria is the most accurate and scientific method. Now the chief point, as it seems to me, on which more light is wanted, is the mechanism of production of the symptoms. Granted that a particular mental state is accountable for the disturbances of function, how are these actually brought into being? Granted that amnesia or absentmindedness [in accordance with Janet's views then being examined] caused hysterical motor defects, why have we tremor in one instance and paralysis in another? And what are the objective features of these? Can we thereby learn anything as to the seat of the functional defect? I am convinced from the study of a number of cases that organic disease will teach us far more about hysteria than vice versa.

Of course, the physiological approach is only one of several. And in directing attention thereto for the moment I do not ignore that which seeks to utilize as much—as exclusively—as possible the assumption of "unconscious mental processes" and of their influence on somatic pathways: nor that other which surveys the hysterical field from the standpoint of more or less conscious processes of simulation. But it is permissible to examine the data without subscribing to any particular theory, and to ascertain whither such study leads. That physiological investigation is legitimate needs no apology whatever; both in former and latter times clinicians have busied themselves therewith, but few if any psychologists—with one noteworthy exception to be referred to later. Kretschmer's recent analysis of hysteria is concerned to a large extent with physiological considerations, though not at all on the lines now to be sketched.

The method chosen no doubt depends on the scientific taste and orientation of the individual physician, and I confess to having been influenced by a teacher who besought me in neurological work never to "invert the pyramid." For a number of years clinico-physiological observation of hysterical phenomena has occupied my time at intervals, and a few of the collected data may now be passed in brief review and their bearing on major hysterical problems examined.

(I) *Motor system.*—Hysterical paralysis is a clinical banality, but study of its intrinsic characters will be found illuminating. It assumes the form of paralysis in rigidity, or of paralysis in flaccidity. Otherwise expressed, the muscular weakness may or may not be accompanied by plain alterations in muscle tonus. When weakness or paralysis is associated with increased tone the condition clinically is usually, perhaps invariably, one of contracture. In flaccid cases the part affected seems emptied of tone, though not always perhaps to the degree met with in atrophic lower motor neurone affections, such as poliomyelitis. All intermediate stages between the "toneless-flaccidity" and "spasmodic-rigidity" extremes may be encountered.

So far as I can discover, my former chief, the late Dr. C. E. Beevor, was one of the first to direct attention to the occurrence in hysterical palsies of the phenomenon known as "defective inhibition of the antagonists." He had under observation the case of a girl aged 18 with incomplete right hysterical hemiplegia, and noted that whenever she was asked to perform a certain movement, the first action detected was that of the antagonist muscles. For instance, on being told to extend the elbow, the first muscle observed to contract was the supinator longus, one of the antagonists to the movement of extension. This was followed immediately by that of the triceps, and there succeeded a confusion of to-and-fro

movements due to alternate contraction of extensors and flexors of the elbow. When she was requested to flex that joint the triceps sprang into contraction first. I was Dr. Beevor's house physician at the time, was duly impressed with the basic significance of this phenomenon for hysteria, and have made it a matter of routine investigation ever since. It is unquestionably the most common motor sign of the affection and can usually be demonstrated with ease. It underlies the vast majority of hysterical disturbances of active motility, being equally remarked in contractures; when the patient seeks to undo a contractured attitude the antagonists will be found to contract still further.

Beevor declared in his Croonian Lectures (1904) that he had never met with this condition of the antagonists acting before the prime movers except in hysterical paralysis, and thought it a diagnostic symptom of that state. Oppenheim also admits its frequency under such circumstances.

The import of this physiological disorder resides in the fact of its obviously constituting a disturbance of the Sherringtonian law of reciprocal innervation, according to which as a given muscle contracts in a normal movement its antagonist is simultaneously de-innervated. In the experimental animal reciprocal innervation holds for all spinal and, more generally, decerebrate reflexes. But Beevor's view of its pathognomonic value for hysteria, though not discounted, must be considered in the light of another fact, viz., that, as was shown in my Croonian Lectures (1925) the phenomenon occurs also in athetosis. In that "organic" affection the orderly innervation and de-innervation of prime movers and antagonists are interfered with. Further, and still more significantly, an endeavour was made in these lectures to show that athetosis results from disordered function of certain *cortical* reflex arcs, and that the underlying lesion may be of cortical site. Another condition attended by precisely the same physiological defect, as I have observed, depends on lesions of the superior frontal cortex sometimes associated with the symptom known as "tonic innervation" and with apraxia. Thus it appears to be of deep interest for the study of hysterical physiology that a special symptom distinguishing it with such constancy is also met with in one or two "organic" states whose site is cortical; and the inference seems fully warranted that hysterical palsies bear the physiological imprint of cortical defect of function.

A conclusion of this kind may appear à priori obvious from the standpoint of theory, but to have reached it on objective considerations alone is surely satisfactory, the more so as it furnishes an instance of explanation of hysterical physiology from the "organic" side.

Another no less interesting motor sign consists in the shunting of the desired innervation to other groups of muscles, not confined to the actual antagonists. This is well seen, for example, in hysterical paresis of the arm; on the request to grasp the examiner's fingers tightly the patient gives the impression of putting forth a great effort, but the grasp remains feeble, while it is easy to be assured of the fact that shoulder muscles and others equally remote from the long flexors are in strong contraction. This "shunting" sign, as it may be termed, is highly characteristic of hysteria, but has its analogies in certain states of muscular weakness following structural lesions—yet under these latter circumstances it is seldom or never so pronounced as in the other.

The fact that both of these physiological traits are such as can be imitated by the normal subject has led some observers (v. Hösslin, Bassett-Jones and Llewellyn) to regard the presence of either as proof of simulation, or at least of an attempt to deceive. But in my opinion this view betrays a merely superficial insight into their meaning. The criterion of imitational capability is worth exactly nothing. With practice the normal subject can so empty his musculature of tonus that a limb can become as flaccid as in poliomyelitic paralysis—indeed, the detonization may proceed so far as to result in actual loss of the knee-jerk, as Jacobson has

conclusively shown. Here is an "organic" condition—loss of deep reflexes—which can be effected temporarily by the aid of "volition" (I regret introducing that highly ambiguous word at this stage, and shall have something more to say of it later). Where, then, is the value of imitation as proof that hysteria and simulation are akin or identical? One might as legitimately claim that atony with loss of a tendon reflex is hysterical and evidence of malingering, since it is not outside the faculty of normal man to reproduce it. The variety artiste on the stage can so deplete his muscles of tone as to give an excellent imitation of a dummy figure, a jointless doll—as atonic and as seemingly "paralytic" as any state of "organic" disease could ever be. With practice, again, a very fair reproduction of the salient features of Jacksonian epilepsy can be made.

The real point, I submit, is that in respect of motor phenomena imitability characterizes more especially those whose physiological seat is cortical, and that symptoms of escape or release at lower levels can be reproduced with perhaps less facility. However this may be—and it is undesirable at present to lay any stress on the generalization—both the "shunting" and the "antagonist contraction" signs indicate, as is here contended, impairment of cortical function, coupled with defective inhibition. The hysteric cannot inhibit antagonistic innervation, nor can he prevent displacement of innervating currents in an erroneous direction.

A word, next, on those forms of motor disability which consist of "positive" movements. Hysterical tremor, for instance, considered physiologically, presents no separate or contrasting features when set alongside those of so-called "organic" type. I have frequently found intention-tremor clinically indistinguishable from that of disseminated sclerosis. The reputed differentia of variability, of influence by psychical and emotional stimuli, of dependence on the attention paid to it, and others, are demonstrably invalid. Numerous "organic" tremors can be affected by a whole series of factors, exhibit most marked fluctuation and fluidity, are highly irregular, shift their incidence, and are aggravated when the subject is under observation. A hundred years ago James Parkinson himself noted the disappearance of the tremor of paralysis agitans in consequence of mere change of posture. As a matter of observation, not a few hysterical movements of this kind sometimes seem as "fixed" and as little variable as those deemed the result of structural lesions. Now it is within common knowledge that hysterical subjects exhibiting such movements do not complain of fatigue, or at least appear to be less conscious of it, than does a normal subject who executes them intentionally; moreover, the Parkinsonian and the torticollic, by way of instance, frequently (though not invariably) admit muscular fatigue and aching. Kretschmer, I consider, is definitely in error when he asserts that "a rapid, rhythmical and somewhat constant shaking tremor, in general, will absolutely not allow itself to be imitated voluntarily under normal experimental requirements, either by healthy or by nervous persons." On the contrary, we can easily convince ourselves of the possibility of imitation by actual practice. But he rightly points out that under the latter circumstances it leads to such a degree of fatigue that its continuance becomes impossible. The difference in this respect seems to depend on the fact that in hysteria, as in "organic" states, tremor is an escape-phenomenon of an infracortical level, and that the experimenter is presumably utilizing neomotor mechanisms to reproduce the activities inherent in palæomotor mechanisms of a lower physiological grade; fatigue sets in more readily in the former case because such artefactive tremor forms no part of their habitual function. At any rate, it seems feasible from a physiological point of view to attribute the "positive" movements of hysteria to failure of transcortical inhibition when their type is high, and of corticifugal inhibition when their type is low.

So far as the multiplex syndromes categorized as the hysterical fit are concerned, their range, from fugues at the one extreme to immobility and lifelessness at the

other, covers so wide a symptomatic field as perhaps to render attempts at synthesis precarious. Reduced, however, to their lowest terms, one and all are indicative of release of function from conscious control. Differences between hysterical and epileptic fits are matters of degree and not of kind. In each, the depth to which unconsciousness proceeds is variable, and if more profound in the average major epileptic seizure may be serviceable in clinical diagnosis but not in nosological differentiation. Both show convulsive and quasi-purposive movements on occasion, the latter predominating in hysteria; and while cyanosis, tongue-biting, and micturition frequently distinguish the one, and automatisms the other, the distinctions resolve themselves into the simple question of which mechanisms are prone to be involved, and which to escape, in either. Otherwise expressed, clinical differences stand for modifications in site and extent, but not for intrinsically or essentially different processes. A general resemblance between the attitude in extensor rigidity of many hysterical attacks and that of the decerebrate animal cannot be denied, for it is a matter of direct observation; moreover, it is to be expected, since if for any reason, through any agency, neuronic control of infracortical mechanisms is in abeyance, these are bound to exhibit on release their specific functional qualities. The physiological characters of some hysterical fits may be taken as evidence of transient decortication or decerebration, nor can I think any other interpretative view permissible. For the student of hysterical physiology the problem is to examine and determine to what extent, down to what levels, neuronic dissociation can be effected by the processes of hysteria.

(II) *Sensory system.*—The empiricist taking the sensory derangements of hysteria at their face value notes the neuralgias and topalgias on the one hand, and the anæsthesias on the other. He is struck by their variety and variability, their capacity for rapid change, and—so opinion has it—their failure to correspond to anatomical schemes; they are alleged to conform with psychical but not physiological dispositions. As illustration of this latter statement we see cases in which the breast but not the nipple is anæsthetic, the front of the body but not the back, and we are familiar with the "glove" and "stocking" anæsthesia of the textbooks.

But ere assuming therefrom that hysteria is a "disease of the mind," a disorder on the plane of mental images, we do well to recall that the physiological arrangement of the mechanisms underlying conduction of sensory impulses varies at successive neural stages. Peripheral loss of sensibility can be distinguished from spinal loss, spinal from thalamic, and thalamic from cortical. In respect of the last of these the clinician can prove from actual experience that a re-arrangement or re-representation of lower sensory schemata takes place, and that in some forms of cortical lesion the distal parts of the opposite limbs are much more affected than the proximal. This fact of itself at once reduces the differential value of "glove" and "stocking" anæsthesia, apart from the other fact that it may be found in syringomyelia, as was demonstrated years ago by Brissaud. Further, as regards the arm more especially, evidence can be adduced which clearly suggests the existence in the cortex of a pre-axial and post-axial segmentation, and errors of reference in either direction can be shown to occur with certain cortical lesions. A front-and-back schematization is not only inherently possible, but is rendered probable by studies of Redlich, Vierheller, and others, in both spinal and prespinal cases "organic" in origin. We recognize the existence of "sidedness" in sensory disorder of the highest level, and that on an "organic" basis: allocheiria or, preferably, dyscheiria, considered distinctive of hysterical states, I have seen characteristically in disseminated sclerosis. Some evidence has accumulated favouring the conception of what may be called a longitudinal segmentation of the trunk in the cortex.

We need not, however, enter at large into details of this kind. The point that emerges is simply this, that in the light of such data it is rash to presume a psychogenic basis for sensory disorders because of peculiarities in their segmental

type when there is presumptive evidence of physiological arrangements in the cortex to explain their occurrence.

Some reference is here desirable to the not infrequent concomitance of hysterical disturbances of sensation with absence of bleeding when the cutaneous zone affected is pricked with a pin. So ancient and notorious an observation as this becomes unusually instructive when set beside a further clinical fact, viz., that precisely the same combination has been seen in connection with "organic" sensory change caused by a lesion in the formatio reticularis of the medulla. I have reported elsewhere the analysis of a case of occlusion of the left posterior inferior cerebellar artery in which the patient discovered for himself that he did not bleed in the analgesic area when the skin was punctured by a needle. I quote from the original record:

> Mr. M. had often noticed that pricking of the left face, in addition to its being felt as pressure merely, never resulted in any bleeding. He had frequently experimented with himself in this connection, and says the same thing is true of the right side of the body. About three weeks ago, however, coincident with the diminution of the "subjective sensations" on the left face, he found that pricking was followed by bleeding for the first time since the onset. I re-examined him from this point of view, and can vouch for the fact that blood is much more readily obtained by pricking on the left hand than on the right, whereas there is no difference now between the two sides of the face.

That some vasomotor change had occurred over the left face and right body and limbs seems certain—presumably a degree of vaso-constriction. The association of the same vasomotor state with hysterical anæsthesia is deeply interesting. I remember a case of complete hysterical paraplegia in a young woman of 22 where the degree of analgesia was so profound that a needle was passed through the calf without its being perceived, and without causing any bleeding. After a single application of the wire-brush the analgesia disappeared and bleeding occurred at once whenever the skin was pricked.

It seems only one conclusion is permitted by comparison of these two cases; an alleged stigma of hysteria turns out to occur also from "organic" lesions of the medulla and loses any specificity it is thought to possess; moreover, the inference can justifiably be drawn, I submit, that bulbar centres and mechanisms are involved in certain cases of hysteria, and that these in part belong to the neuro-sympathetic system.

(III) *Reflex system.*—Anyone with clinical experience will allow that reflectivity frequently exhibits departures from what is normal. In hysterical hemiplegia or paraplegia the observation is now old and well-established that the plantar response is often lost; with repeated stimulation no reaction is obtainable, and this, too, when the foot is neither specially cold nor anæsthetic. I have been familiar with this for many years, as also with the fact that the abdominal reflex may be reduced (or even lost) in hemiparetic cases usually in association with sensory diminution on the same side—an observation substantiated by Monrad-Krohn. Of the occurrence of hysterical ankle clonus no doubt can be entertained. Interference with sphincteric action, too, needs no comment; incontinence of urine was present for six weeks in the case of a hysterical paraplegic under my care, and retention is no rarity.

Dr. C. S. Myers is the psychologist referred to above who, almost alone of his class, has paid any attention to these phenomena, or evinced appreciation of their importance. At the end of the War he said that "in this country at least we have been paying so much attention to the mental aspect of the war neuroses that a detailed examination of the accompanying bodily symptoms has been generally neglected." His own observations showed him the frequency with which the plantar reflex fails, and he also remarked in many cases of asymmetry as regards the two that both knee-jerk and abdominal reflex appeared weaker on the same side as the feeble flexor or abolished plantar response, and that diminished appreciation of cutaneous stimuli was usually in evidence also.

I long ago satisfied myself that distinctions between "organic" and hysterical

ankle clonus formerly relied on could not be trusted; Babinski's criterion that the former is present each time the patient is examined, whereas the latter varies and may not be elicited on occasion, must, from my personal experience, be considered valueless. Nor does irregularity of rhythm carry any differential weight. Now if diminution of the abdominal reflex is depended on as an early sign in frontal tumours, disseminated sclerosis, and pyramidal conditions generally, I cannot see why the same phenomenon in cases of hysteria should not bear the same meaning or import. It is unnecessary now to advert to the rather disputed question of the development of an extensor plantar reflex in hysteria, but loss of the plantar reaction must signify some physiological change. A similar reduction characterizes many cases of "organic" hemiplegia at the acute stage, and according to Ganault the reflex is completely abolished in 10 per cent. No reason whatever can be advanced for accepting these physiological specialties in "organic" affections and denying them equal significance in cases of hysteria.

For simplicity's sake a few comparatively common, everyday symptoms of hysteria have been selected for examination from a neuro-physiological angle. This sketchy and compulsorily limited review has perhaps sufficed to demonstrate how cortical, infracortical, mesencephalic, bulbar, spinal and neuro-sympathetic mechanisms may severally be disordered in function as a result of processes which we call hysterical. No doubt in one sense this is a mere platitude; for after all what others are there for hysteria to usurp than those of the person concerned? But it is something, surely, to be able to show that differentiating criteria as between organic and hysterical conditions have lost much of their specificity, that symptoms thought exclusively hysterical reappear under circumstances never assigned to the interference of the psyche, and that many of the somatic manifestations of that "neurosis" have their counterpart in known physiological derangements of one grade or another. In one at least of its aspects the affection becomes less mysterious when its activities can be traced through different physiological levels.

The progress of medical knowledge has been so gravely hampered by persistent use of the two terms "organic" and "functional" that it is high time they should be discarded for ever. Scarcely less objectionable is the alternative antithesis of "structural" and "nutritional." (I have studiously avoided in this discussion the word "functional" even as reputedly synonymous with "hysterical.") In their place, if terminology is required, we may with advantage employ the pair of opposites "static" and "dynamic." It must be clear on due consideration that innumerable nervous symptoms stand for dynamic alterations in function which cannot at present be correlated with any recognizable lesions. In the case of a major epileptic fit manifesting itself all over the body, so to speak, no one can imagine for a moment that there are corresponding "lesions" all over the nervous system. The display is a physiological reaction to some nociceptive excitant whose site of initial action is probably extremely limited, but a dynamic, and transient, extension follows over a wide region of normal nervous tissue. In a number of disease-conditions associated with static lesions the symptoms themselves exhibit fluidity of the most obvious kind, as has already been alluded to in connection with the tremors of paralysis agitans. How then can we link them to the cellular changes we detect under the microscope?

Applying this general semeiological conception to hysteria, we note at once the prominence of the dynamic and the comparative absence of any static elements therein. We are impressed by the strictly physiological inhibitions and excitations of that state and by their ranging over higher and lower mechanisms alike; but at the same time their essentially unfixed and fluid character stands out saliently. How can we explain the rapid cure of hysterical disabilities—or shall I say their clinical disappearance—how understand that nervous mechanisms are, as it were, ready to resume duty at a moment's notice, after perhaps some years of disuse, unless on the hypothesis that function is abrogated dynamically but not statically? There is a

block somewhere, a pure inhibition, in the case of negative symptoms; or, on the other hand, inhibition is removed and release-phenomena come into being as positive symptoms. Neither can be correlated with lesions of a static kind, but that physiological derangement of a dynamic character is invariably present seems almost self-evident, and from the illustrations already furnished may be considered objectively proved. The difference, then, from so-called "organic" conditions does not reside in the co-existence of static change, for this need not accompany all the manifestations of that class, but rather in the manner of onset of the symptoms and the manner of their removal.

We can trace through the symptomatological diversities of hysteria the action of ordinary physiological processes, precisely the same as are encountered in the dynamic symptoms of affections we categorize as having a basis in recognizable disease of tissues; but as soon as we approach the question of their origin and pathogenesis difficulties accumulate. In these days a majority of psychiatrists and neurologists presumably adopt the view of their ideogenic origin, and regard this as almost axiomatic. Perhaps the most commonly accepted theory is that they are conditioned by one or other kind of sexual conflict, of which, to take concrete examples, some may be enumerated as follows: jilting in love, jealousy, lovers' quarrels, a sister's marriage, fear of pregnancy, marital unhappiness and so forth. To enlarge the catalogue would be both easy and superfluous. Frankly, this strictly sexual ætiology appears incapable of universal application to questions of hysterical pathogenesis. Why and how such psychical incidents should produce loss of the plantar reflex, or local vasoconstriction and cutaneous anæsthesia, eludes comprehension. On the view that hysterical symptoms are nothing else than reactions to stimuli, it still is difficult to understand why psychical excitations of this completely restricted sexual kind should be capable by themselves of evoking responses ranging from fugues to retention of urine. With some knowledge of the extensive psychological literature on the subject I have not met with any serious effort to correlate ætiology and symptomatology amid its profuseness. Between the one and the other stretches a pathogenic hiatus of a glaring kind, which cannot be said to facilitate acceptance of the sexual theory.

If the ætiological net is cast a little wider, we might adopt the hypothesis that hysterical reactions are determined by the emotional life in an unrestricted sense. Emotional experiences and impulses, originating in whatever fashion, associated with sexuality or not, do unquestionably help to engender the development of hysterical syndromes; they may be taken as exciting, if not predisposing causes. It is, perhaps, easier for the trained neurologist to comprehend the physiological effects of emotional disturbance, since he has at least a little knowledge of the mechanisms of the neuraxis underlying the expression of the emotions. Radiation of emotional effect can be translated into anatomico-physiological terms: the somatic and neuro-sympathetic accompaniments of emotional action range widely and are capable of objectivation. Varieties of shock have their reverberation in known high and low level neuronic systems. Nevertheless individual hysterical reactions, monosymptomatic types, are not easily correlated with the causative action of so *general* an excitant or inhibitant as emotion. Of course I recognize and for that matter have myself observed the occurrence of hysterical symptoms (such as aphonia or amaurosis, for example) in which it has been feasible to link the *form* of the reaction to some pre-existing incident connected with the particular part of the body affected, but in numerous others it is impossible to trace any such association. A comprehensive study of hysterical semeiological types in relation to ætiological variants is urgently needed.

The assertion that we are all potential hysterics, often put forward both before the War and since, is explained by Kretschmer to mean that everyone carries within him old, instinctive, primitive forms of reaction more or less covered up and

controlled by the acquisitions of culture. Most of those who have had experience of hysteria will agree that it is apt to appear at certain physiological periods under circumstances of an emotional kind. Yet at times it undoubtedly arises unexpectedly; I have seen hysterical hemiplegia in a King's prizeman at Bisley. To the generalization, however, it is impossible to give formal consent; on the contrary, I submit that the evidence favours the view that the hysteric is born and not made, and that an unstable constitutional background, a "temperament," if the word is preferred, is the soil from which hysterical growths spring. And it seems feasible to suggest that this determinant may be in reality of a physiological and not a psychological kind—that it is constituted by an inherent lability of reaction, a lack of neuronic cohesion and firm integration, an abnormal facility in dissociation of neural systems, such as undoubtedly characterize hysterical semeiology from the viewpoint of nervous function. When we are told that the "acquisitions of culture" cover up the "primitive" within us, it appears to me preferable to say that transcortical inhibition dominates the neuraxis; when the "hypoboulia" of the hysteric, his weak will, is paraded as explanatory of hysterical pathogenesis, a physiological exposition of the data should, in my view, be sought; we might speak rather of failure of one cortical element to inhibit another—a state of affairs the extreme likelihood of the occurrence of which is postulated by Sherrington for various fields of cortical action. That "volition" seems constantly, or at least repeatedly, to take a share in the production of hysterical symptoms is notorious, and is responsible for the not unnatural view that simulation enters largely therein; but it is possible that the physiological basis of the "will" is inhibition; that a "voluntary" movement signifies merely one which is transcortically permitted; that "letting go" rather than "doing" represents the true meaning of a "volitional" act. With a conception of this kind, developed along physiological lines, the peculiar features of hysterical motor disorder receive a simple explanation; we do not mix up a psychological impairment—a weak will—with a physiological derangement—defective inhibition of antagonists—but take the former to signify failure of transcortical control and elucidate the latter thereby. An ingenious explanation, on purely physiological grounds, of the phenomena of hysterical palsy was published by Graham Brown and R. M. Stewart in a paper which appeared at the end of the War and seems not to have attracted the attention it certainly merits.

The general tenor of the argument here outlined with some restraint is that physiological processes lie behind nervous manifestations at all levels; that the cortex, considered as a ganglion, cannot differ inherently in function from other, infracortical, ganglia except as regards complexity; there is no reason to suppose nature makes a jump from one order to another totally different at the cortical stage. Reflex actions are there to be expected, in analogy with those located inferiorly. The present trend of physiological research is to reduce steadily the number of functions once ascribed to "volition"; for example, mechanisms controlling posture and balance are now taken away from it and assigned to reflex arcs independent of the higher levels. So far as the cortex is concerned, I am by no means alone in arguing that much cortical activity partakes absolutely of a reflex character; and I believe that what for want of a better expression we term the "will" is being driven from one transcortical ditch to another as it struggles to survive. It seems logically sound to seek to interpret cortical activities in physiological terms alone, and to avoid use of the psychological term "volition" altogether. Admitting that many of the phenomena of hysteria belong obviously to the highest grade of activity, are so like "volitional" actions as to be thought indicative of deception or simulation, it is suggested they represent transcortical disorder of function, on the strict analogy of functional release at lower levels. An approach from below upwards, as it were, has much to commend it, for the gap between physiological and psychological systems is not likely to be bridged from the psychical side.

Section of Orthopædics.

President—Mr. P. JENNER VERRALL, F.R.C.S.

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PRESIDENT'S ADDRESS.

Some Amputation Problems.

By P. JENNER VERRALL, F.R.C.S.

IN the early part of this year Mr. Max Page opened a discussion in the Section of Surgery with an able but brief paper on "Amputations," which was intended as an introduction to the subject as presented by the limb-fitting surgeons of Roehampton. The meeting was only fairly well attended, no orthopædic surgeon other than myself was present, and no discussion of the subject was possible, owing to lack of time.

I felt then that the subject was by no means exhausted, and that although, obviously, amputations must be considered as general surgery, in so much as they cannot all be performed by orthopædic surgeons, the latter should have the last word, and accordingly I make no apology for reopening the question from the standpoint of the surgeon, and, in order that the Section may gain a real advantage from this meeting, I beg you to follow my address with a discussion. In addition, some of the points raised at the previous meeting, although not discussed at the time, have been made the subject of correspondence in the medical press, and I shall take the opportunity afforded by this occasion to reply to these criticisms both on my own behalf and that of my Roehampton colleagues, Dr. Langdale Kelham and others.

Perhaps the most trenchant criticism that reached us was that we were speaking only of war amputees, and that our views were valueless for civilian cases. I admit that there is in the majority of war cases an element of chronic sepsis previous to amputation absent in most accident cases in civil life, and it would be idle to deny that war cases (as, indeed, many civil cases) must be judged from a general economic and not a purely surgical point of view.

However, none of us deal exclusively with war cases, and we have our civil practice, hospital and private, and it is at least worth while to give others the benefit of the experience derived from the very large number of amputations that have passed through our hands. It is also only fair to remember that accidents necessitating amputation occurred to serving sailors and soldiers, in every way surgically identical with those in civil life.

I have called this paper "Some amputation problems," and I propose to deal in the main with the unusual. However, I think it will be better, and make my subsequent remarks more intelligible, if I state briefly what is generally accepted as the normal and the ideal in amputation stumps. In the lower limb a tilting table prosthesis is to be avoided if possible, but must be fitted to a stump of less than 5 in. measured from the great trochanter. In general, the best amputation for this limb is one just below the small trochanter in which the psoas flexes the stump and the patient sits in the bucket. For an above-knee limb the amputation should be at least 4 in. above the condyles and, preferably, should leave a stump measuring 10 to 11 in. from the great trochanter, where the normal femur measures 19 in., 12 in. if the normal is longer. The ideal below-knee stump contains 7 in. of tibia, although much shorter stumps than this can be fitted. Greater length in the leg is useless and harmful. In the arm the ideal amputations above and below the elbow are 7 in. below the acromion and olecranon respectively.

As a result of increasing consultation and co-operation between operating and limb-fitting surgeons it is now accepted that flaps should be no longer than the diameter of the limb, and should contain no more muscle in their base than may be

needed as sheer tissue solely to ensure the blood-supply. It is obvious that it will be necessary to employ a thicker flap in an attenuated and ill-nourished limb: I shall, however, return to this presently.

Next, as nerve troubles were once (if they are no longer) the most frequent of amputation problems, it is absolutely essential that agreement should be reached as to whether or no any point of operative technique is of value. Mr. Max Page is in favour of dealing with the major nerves by crushing and tying with a minimum of traction. With this I agree, but he goes on to advise alcohol injection with the very reasonable idea of cutting off the pain effects in the early days after amputation and obtaining an earlier settling-down of the sensitive reflex. Since hearing his paper I have been considering this point very carefully, and have come to the conclusion that, although the immediate effect is as good as Mr. Max Page claims, alcohol-injection produces a perineural fibrosis, which is bad in the long run. I should like to hear the views of Members on this point, as it is of the highest importance. Hæmostasis should be complete, and there should be no hesitation in surrounding small portions of tissue with a circular ligature if (as so often happens in re-amputations) there are patches of small vessels which cannot be picked up singly. Hæmostasis being complete, I advise that no drainage be employed. I have come gradually to this conclusion during the past three years. It is still regarded as an unorthodox practice, although Wilson in America agrees [1]. I would far sooner stitch up loosely, allowing space between sutures for the exit of oozing than introduce a drainage tube which functions for a few hours at most, and like other doors can be passed through in two directions. If bandaging be careful, a severe hæmatoma, needing evacuation and re-suture, is of the rarest occurrence. I think most surgeons will agree that the amputation most liable to hæmatoma is the one that bleeds very little at the time of amputation.

Both to give rest and to prevent flexion deformity, below-knee amputations should be splinted, and in above-knee cases the stump should be steadied by a light sand-bag placed above—and not, as so often seen, below—the stump, the latter practice being very conducive to the early development of flexion deformity.

My cases are not dressed until the fourth day unless there be any special indication for doing so, and the patient must remain in bed for at least three weeks. Massage when the stump is normal is, in my opinion, quite useless, and may even be harmful, as militating against that rest and settling down which are so essential.

Re-amputations are more difficult than primary amputations owing to the pre-existent scar, anomalous vessels, and often to the general congested and varicose condition of the parts.

In the discussion on this subject earlier in the year, by common consent no mention was made of emergency amputations, or special amputations, the intention being to describe the normal. I propose now first to deal with the former of these and then with the abnormal. There are three varieties of emergency amputation, the guillotine, the through-joint and the amputation with flaps left open. The last is but rarely required, for two conditions are essential to its use: the sepsis that is feared must be comparatively mild and the length of limb that can be preserved must be so short that by no other means can the joint above be permanently retained. As these amputations are generally required on account of sepsis, the one consideration will be the avoidance of the opening up of fresh tissue, while providing the maximum of drainage, and, in this respect, the guillotine is superior to the through-joint, as the recesses of the synovial cavity are potential lurking-places for sepsis long after it would seem to have subsided. Undue retraction of the skin will be prevented by some form of extension, such as the admirable method described by Elmslie in his "After-treatment of Wounds and Injuries" [2].

As a dressing I have found the spraying of the raw surface with dichloramine-T superior to all other methods; it is antiseptic, analgesic, non-adherent and nice-smelling.

Re-amputation must be deferred until all sinuses have been healed for at least three months, and there is no œdema of the stump, but not necessarily until the wound is healed or all sequestra have separated. One will always tend to err on the side of waiting too long, and it often occurs that, in the case of thigh amputations, while waiting, the original amputation heals so well that no further amputation is needed, and even the nerves, which have not been cut short at the operation, give no more trouble. In operating in the presence of an unhealed wound it is obvious that thorough carbolization of the ulcer is essential.

Before proceeding to deal seriatim with the various problems that arise in regard to stumps, I would ask your permission to express certain personal opinions on certain amputations and would invite criticism. Taking operations in anatomical order, it would appear that on the whole the Lisfranc group and the Chopart have met with fairly unanimous disapproval. I think that this, although generally true, is a little too sweeping. In the Lisfranc the one disadvantage is the loss of the long arch of the foot, and I have frequently seen such cases unsuccessful because the patient was wearing a boot with a blocked end and no arch-support. The only way to fit such a case is to take a plaster cast of the stump, add an imaginary piece to represent the lost portion, and make a full metal arch-support reaching from heel to toes, the missing portion being represented by a block, faced with sponge rubber towards the end of the stump. With such a mechanism a Lisfranc type is a good amputation.

In the adult the gastrocnemius is so strong and the patient's adaptability to new muscle-balance so poor that a Chopart is a bad operation, but in the case of a child, say, a boy playing in the street, the front part of whose foot had been run over and destroyed, if the tibialis anticus, and preferably the toe-extensors be re-attached, a most useful foot can be obtained and one needing no prosthesis, a matter of concern for the poor.

At the discussion above-mentioned all the speakers, operators and limb-fitting surgeons condemned the Syme from experience.

The reply of my colleague, Dr. Langdale Kelham and myself to the criticism since made is that we do not deny the existence of many successful Symes both civil and military, but we are speaking of the generality of cases, not of exceptions, and a Syme is far less certain of remaining permanently satisfactory than is a mid-tibial. Briefly, the defects which commonly arise are circulatory, displacement of the end-bearing surface and diminution in its size, so that it will no longer suffice to cover the bone-end, even if replaced by operation, keloid and painful scars, splitting of scars from constant traction, hypersensitive areas and pin-point neuromata, callus-formation, rarefaction of bone with bone-pain and periostitic nodules on the tibia. It has been said that an unsatisfactory Syme is a Syme badly done, and that one should follow Syme's original method, but as this would involve a stab-hole through the flap for drainage, I do not think it can be taken seriously. At any rate, I have seen many Symes go wrong which had been performed by surgeons known to me, whose skill is beyond question, and in civil cases as much as in military.

It is generally admitted that the mid-tibial amputation should leave a 7-inch tibia and a slightly shorter fibula but the situation of the flaps is debatable. If unhampered by scars, etc., or circulation, I think lateral flaps are a mistake, as the scar tends to pucker between the bones and become subject to the intertrigo, of which I shall speak later, and the scar is peculiarly liable to splitting and ulceration from skin-traction.

In a muscular and well-nourished leg, an anterior skin-flap is good and will not be pulled upon by muscular action, but in atrophic legs, especially in old sciatic injuries, where the circulation is none too good, I prefer to make a postero-external flap calculating the length so that after shrinkage the scar will lie transversely $\frac{1}{2}$ to 1 in. below the tibial level. The skin should be retracted upwards before the anterior transverse incision is made.

I have, above, condemned the Stephen Smith as a temporary measure, but as a permanency it has no surgical defects, only the limb-fitting ones of needing a heavy limb with a difficult external knee-joint.

In the thigh there is no advantage in a very long stump as it may interfere with the artificial knee or suffer from circulatory troubles, and as the psoas is the chief motive-power for its flexion, the preservation of great length will not improve the leverage of this muscle.

In amputations through and near the hip-joint it is important, in deciding exactly how much of the femur to retain, to take into account the mass of the soft tissues, because the greater this is, as e.g. in a fat woman, the more essential it is to retain some sort of skeleton in the interior of the stump to give stability to the tissues.

Passing for a moment to the upper limb, in the fore-quarter amputation, which is, of course, rarely indicated, from my own experience I cannot understand why the inner end of the clavicle is retained in the classical amputation. If it be removed, the sternal head of the sterno-mastoid remains and the tying of the subclavian vein (the only difficult part of the operation) is much easier if done further inwards where it is less encumbered by tributaries and more room is available. Also it would appear to me that in theory, at any rate, the removal of the latissimus dorsi should be very complete as its tendon actually enters the area most commonly affected by the tumour, for which such operations are mainly performed.

In operative technique it will be found that previous injection of the brachial plexus with novocain does much to diminish post-operative shock.

I will come now to the more direct consideration of amputation problems.

Let us first consider stumps whose only defect is their shortness, and where our effort is directed towards the retention of a joint. The short thigh-stump is frequently spoilt by excess of soft tissues, which have often a poor circulation. Such a stump should be thin and conical and I have frequently to perform somewhat crude operations on these stumps, consisting simply in the removal of superfluous masses of flesh. Even the situation of the scar is relatively unimportant compared to the general shape of the stump. In the leg the absolute minimum tibial length is $1\frac{3}{4}$ in. It is remarkable how some individuals manage to control a short leg-stump and some do not. It is again largely a question of redundancy of tissue, and the removal of all muscle (mainly the gastrocnemius) from the back of the leg will often enable a limb to be fitted.

If the knee cannot be retained, it will be necessary to amputate through the thigh if a modern limb is to be fitted, and this is quite reasonable in the case of the war-wounded, for whom the Government is quite prepared to provide and maintain the best prosthesis. In civil life, however, where the money is not forthcoming, the old-fashioned kneeling peg-leg is not to be despised and a serious consideration of the case from an economic stand-point is advisable before re-amputation.

It will be in these cases that the question of excision of the fibula will arise. In general the retention of the head of the fibula is advisable in spite of any bursæ that may form, as it provides an excellent anchor for limb-fitting, standing pressure well. In the rare case where the end of the fibula has rotated round to the back of the stump and the tibio-fibular joint is loose, removal of the whole bone is essential. If the fibula be removed, experience shows that at least six months must be allowed to elapse before any limb-fitting can be attempted, as the surface left after removal

stands pressure badly. However, it is just in these short stumps that removal is justifiable, as the stump will be neater and a tuber-bearing limb inevitable in any case.

In the upper limb, in an intelligent and willing patient, a short upper-arm stump can often be rendered useful by the division of the latissimus dorsi, pectorals, etc., and plastic treatment of the skin.

I propose now to consider unsatisfactory stumps in general and I will begin by saying that a large proportion of trouble is caused by too early limb-fitting. A perfectly clean amputation in which sepsis has either never been present or has been prevented from development by primary amputation, may perhaps be fitted with a prosthesis in three months, but in war cases, when sepsis has certainly been present and in secondary amputations in civil life, six months should be allowed to elapse before limb-fitting is attempted. Thus both the bone and the nerve ends have had time to settle down. There is a chronic periostitis which tends to persist if a limb be fitted too soon after an amputation near a septic focus.

As regards the use of pylons or other temporary apparatus, I have already expressed my views, namely, that below-knee pylons are very unsatisfactory and that above-knee pylons, although surgically bad, are economically good, as saving much limb-fitting and alteration of the bucket. It is essential, however, in such cases that the pylon be fitted by the limb-maker, under surgical supervision, on limb-fitting principles, reproducing exactly the pressure points, etc., which will obtain in the permanent prosthesis to be fitted later.

It is found that the lack of cutaneous nerve supply to a stump with consequent anæsthesia and trophic disturbance proves an insuperable barrier to fitting. Apart from actual trophic lesions, the patient cannot appreciate minor discomforts in his prosthesis, and these progress insensibly to the production of ulcers. It is surprising, however, to find what a large overlap of cutaneous sensation really exists, and stumps often retain their sensation when, by all the anatomical description of nerve-supply, they should have lost it.

Let us now consider the various structures in a stump and the troubles from which they may suffer, beginning with the skin.

Many people suffer from seborrhœa and a tendency to acne. Such people will tend to be troubled with sebaceous adenomata on their stump. There is a constant contact between the greasy skin and the stump-sock which impedes the free discharge of the sebaceous material, and with the addition of staphylococcic infection furunculosis develops. This is especially the case with thigh stumps, the condition generally developing on the inner side. If the patient ceases to wear the limb for a time and if appropriate vaccine treatment is given, the condition will subside, but this does not ensure a permanent cure.

Unless the adenomata are very large, removal is inadvisable as the resultant scar is a serious defect. If operation be called for, it is better to excise the whole area of seborrhœic skin and not merely the cysts. This, at any rate, gives the stump a fresh start. Otherwise, the use of white precipitate ointment (1 in 10) regularly will generally keep the condition in check, but, except in the case of very seborrhœic skins, it will generally be found that where cyst-formation occurs there is some defect in the limb-fitting which can be remedied and the routine use of the ointment is not a serious hardship.

Naturally, from time to time one meets cases of generalized psoriasis and the disease may affect the stump and entirely preclude fitting, but a far commoner condition is one that is clinically an eczema, but, in my belief, really a septic dermatitis, as in such cases it is the rule to find that there is a deep focus of infection in the stump, periostitis, etc., the treatment of which will cure the disease. Occasionally a small foreign body surrounded by subacute sepsis in the soft parts may be the cause.

And then there is intertrigo, the constant contact of two perspiring skin-surfaces. The ill-effects of this are best seen when the amputation scar is puckered, or there have been previous ill-advised attempts at cinematization, but, even in a normal stump, where the fit is bad, there may be folding of the skin inside the bucket. All infolded scars must be freely excised and great care must be exercised in the subsequent suture and limb-fitting.

A scar adherent to the underlying bone causes greater trouble in leg than in thigh amputations; indeed, in the latter it is generally of little importance, as, the weight-bearing being taken from the tuber-ischii, there is relatively little pulling on the skin in walking, if the limb-fitting be good. An adherent scar in the leg is best treated by excision, a small piece of bone being sacrificed, if need be, to ensure non-adherence. Massage may serve to separate slightly adherent scars in the early stages, or occasionally a tenotome may be used. Such scars may be the cause of recurrent ulceration, the wound being pulled open by the skin, or bad limb-fitting may produce the same result, even when the scar is a good one, and even good limb-fitting may fail to avoid ulceration, when the scar has been placed in a faulty situation.

However, commoner causes of ulceration are: (1) Deficiency of circulation, either from too great length of stump, or from one of the more general causes that I shall mention later. (2) Anæsthesia, either associated with trophic defect, or permitting minor traumata to pass unnoticed. (3) Such general diseases as syphilis, acting either in tertiary form, or from the production of tabes, etc. (4) (Rarely) pure nervous disease, e.g., syringomyelia.

Treatment will follow the appropriate line.

The formation of bursæ over pressure-points, best seen round the top of the leg in below-knee stumps, is not in itself a defect—provided the size of the bursæ be not too great—as it is a natural process. For some years I was in the habit of excising troublesome bursæ, but now do so very rarely, as the resultant scar is as troublesome as the bursa, one cannot guarantee that the bursa will not reappear, and accurate limb-fitting should absolutely prevent such excessive growth.

Let us now consider problems connected with the bone. In war cases, very frequently, and in civil cases occasionally, amputation of a limb must be performed through a bone which has been the subject of chronic osteomyelitis, either generalized in the bone or round a compound fracture. All amputations should, if possible, be made through sound bone above the old fracture, even at the cost of loss of length, as latent sepsis is a potent source of trouble. When this is impossible, it is reasonable to treat the osteomyelitis in a stump just as in a normal limb, by trenching, etc. This latter operation is also good for the rare cases of true bone-pain, seen mostly in thigh-stumps.

Much ingenuity has been used in the treatment of the bone-end in amputation with a view to preventing the formation of spurs. My own experience is that no special treatment is necessary, and that spurs will form quite irrespective of the methods used. They seldom give the least trouble—even the large and common postero-internal spur on the thigh—provided they are situated in some other place than directly under the scar. Their excision is, therefore, rarely indicated.

I come now to a problem, the treatment of which is certainly a controversial question, and I shall be glad to hear your opinions. I refer to stiffness of joints.

In the case of the hip, ankylosis, in good or bad position, is next door to an absolute bar to the fitting of a satisfactory limb, although I anticipate that it will be said that a limb can be fitted and that the patients will be no worse off than if they had an ankylosed hip with a perfect leg. I maintain, however, that these are worse off than with a tilt-table. The alternatives are, therefore, to re-amputate to give the best stump for a tilt-table, or to attempt the formation of a mobile joint. It would appear that, as no weight has to be borne on the joint, a simple

excision of the hip would suffice, but experience has shown that this is not satisfactory and that the patient gains no control of the prosthesis. It is the fulcrum that is lacking and the preservation of this by arthroplasty makes all the difference. In my experience arthroplasty of the hip in an amputation case is excellent, as the ne-arthrosis has relatively little strain thrown upon it.

Osteo-arthritis occurs, not uncommonly in such hips and will receive the normal treatment. I would only say that arthroplasty or such partial operations as cheilotomy are more promising in stumps than in complete limbs. Partial limitation of movement, such as flexion and abduction deformity, will be treated by massage aided by mechanical stretching of contracted structures. If these methods be unsuccessful, an operation of the Souttar type, even including free capsulotomy, may well be needed.

A hopelessly flexed hip should be left flexed and the stump shortened to allow for the fitting of a tilt-table. The longest stump that can be so fitted is one of 6 in., but this is very unsightly.

Considering, now, the knee: It has been contended that any knee short of a perfect one is not worth retention. With this I disagree, but am open to conviction. A knee that will move well and painlessly from full extension to 135 degrees, provided no tuber-bearing be needed, is of value to its possessor and if, as so often occurs, the limitation of flexion is due to quadriceps scarring and contracture, the wearing of a limb is likely to improve the range of movement rather than the reverse. Flexion deformity of the knee should be prevented by splinting, etc., and in its minor degrees is easily curable by splinting, massage or even tenotomy. In very obstinate cases division of all the structures in the popliteal space may be tried, but, in my experience, this is most unsatisfactory. It is better to re-amputate or to shorten the leg for the fitting of a kneeling peg.

At one time the treatment of neuromata would have been considered one of the most important problems. To my mind it has become less and less so. I have given above my views as to the treatment of the large nerves. If trouble occur later from neuromata, it is the small nerves that cause it, notably internal and external saphenous and small sciatic in the leg, and internal cutaneous in the arm. Previous sepsis makes neuromata more tender, a fact which may account for their giving greater trouble in war cases, though, as we have no instrument for the measurement of pain, it would be absurd to deny that one does occasionally meet with war cases in which outside considerations may influence the patient. Other contributory factors will be such general causes of peripheral neuritis as alcohol, syphilis, etc. In any case, indiscriminate removal of neuromata is to be deprecated, firstly because good limb-fitting will generally suffice, and also because any interference with the nerve will, naturally, initiate a further period of "settling down" for the central reflex.

Operations for a painful neuroma should be local; division of the nerves higher up does not always cure, for some reason or another, and this is especially the case where an attempt has been made to treat both anterior and posterior tibial neuromata by the division of the sciatic in the thigh.

Circulatory defects in stumps are, as I have said, commonly due to excessive length or excessive volume of soft tissue. They may also be due to true deep-seated circulatory defects or to cold. In considering these, one finds that stumps do not differ from normal limbs in being subject to functional and organic arterial insufficiency, such as Raynaud's disease or endarteritis obliterans. Varicose veins or a combined deficiency such as thrombo-angeitis obliterans may also be present, but in certain stumps there is certainly a vascular upset which is nervous in origin and exceedingly difficult to cure.

Two types of operation, both when performed by myself and in cases operated upon by colleagues, have produced temporary, immediate relief—but only temporary—

relapse inevitably occurring in the course of a few months. I refer to peri-arterial sympathectomy and rami-section. I have seen the latter lead to rapid healing of an obstinate stump-ulcer, only to find the scar of a previous sympathectomy break down and remain unhealed. Leriche, in Nelson's "Loose-Leaf Surgery" [1] speaks of such cases and of having found an area of congestion in the spinal canal. I have no experience of this or of treatment of these cases by posterior root section or chordotomy. In my experience posterior root section as a cure for pain in the upper limb, has been a complete failure. I hope that others will give the meeting the benefit of their experience in this matter.

I have twice operated successfully on femoral aneurysms in thigh-stumps, with subsequent limb-fitting in both cases.

Causalgia in a stump is as unsatisfactory from the point of view of treatment as it is in a whole limb, and, again, in my experience, rami-section gives but temporary relief. However, I am more and more convinced that the successive re-amputations, of which one sees so many in these cases, are definitely harmful, and I refuse to do them, although the patient may beg for them. Time and occupation are the only cure, and with experience and the lapse of time one has seen these very tragic cases steadily improve.

The phantom limb is a similar problem and operations are to be avoided, time and occupation and, especially, limb-fitting being our best aids in treatment.

Jactitation of the stump is a real problem, and may occasionally absolutely preclude the fitting of a prosthesis. Although fitting usually improves the condition at first and one is tempted to fit early, this is a mistake, as relapse occurs, and it is better in these as in all other cases to err on the side of waiting too long before fitting, in order to give the nerve centres time to settle down. Treatment may, however, do some good, and careful search will often reveal the presence of some tiny painful neuroma, pressure on which acts as a trigger to set in motion jactitation of the whole stump. Its removal is indicated. Again, in certain cases it is noticed that the clonic contractions are confined to a certain group of muscles, such as the quadriceps in a thigh-stump, and I have had good results from the resection of the anterior crural nerve in such cases. Similar resection of the superior gluteal has been, in my experience, less satisfactory. Rest is all-important, and this may be rendered more complete by the fixation of the stump and the adjoining articulation in plaster for a prolonged period.

Mr. Muirhead Little, in his admirable book [3], mentions the existence of pain felt in a stump during defæcation, micturition, etc. This is not at all uncommon, and the reverse is also true and very troublesome, pain felt in the rectum or bladder when a limb is worn, either being of course due to the unstable nervous reflex. Time is often the only cure, although in some cases pain felt on micturition may be due to bad limb-fitting, the perineal sweep of the bucket being carried too far up. The bucket-edge should be lowered and a true bearing on the tuber-ischii obtained, with weight-bearing slightly more diverted to the gluteal region than is usual.

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Discussion.—Mr. E. MUIRHEAD LITTLE said it was a source of gratification to him that the war-time decisions on the various points related to amputations, arrived at at the Roehampton Hospital, had nearly all been upheld. He now found, on listening to this address, that he scarcely differed from the President on any point.

The President had begun with a consideration of the foot, and he (the speaker) assured him that his improvement in the treatment of the foot was a very valuable one, and if he (the speaker) were now dealing with such cases he would certainly adopt it. The Chopart

was a very good operation if one was not intending to fit an artificial foot; its demerits were only evident when fitting was attempted. He agreed with what had been said as to the length of stump below the knee.

With regard to the Syme amputation, he was still rather unrepentant about that operation; but there was no gainsaying positive facts. The President, and others, who had been working at Roehampton since he (the speaker) had left seven years ago, had found difficulties with the Syme, and it was of no use against that fact to set the advantages which some claimed for the Syme. It could be said that a good Syme was excellent, but a bad Syme was worth nothing. He reminded members of Huggins' book on amputations, in which the author had laid down an excellent way of treating flaps resulting from the Syme after-operation. That little book contained a good deal of valuable matter.

When fitting with a tilting table was intended, he agreed that the best course was to amputate through, or just below, the lesser trochanter, giving in this way something for the patient to sit upon more than the bare pelvis. There had been one or two cases at Roehampton, while he was there, in which the surgeons had to report to the Ministry that they could not fit them; they were cases of ex-articulations of the hip-joint, and the only part left for the man to sit on was too sensitive to bear the weight of the body. If amputation had been done through the lesser trochanter there would have been left 3 or 4 in. of flexed femur to take the patient's weight. If there happened to be any infection of the joint, that rendered necessary ex-articulation.

On the subject of stiff joints, he agreed with Mr. Verrall; not much movement was wanted in order to make the joint useful. The President had exactly indicated the important point: excision took away the fulcrum, and then the limb was not of much use.

As to painful stumps, sometimes they were a bugbear. Mr. Verrall had not mentioned an operation on the upper extremity which he (the speaker) had seen at Roehampton on two occasions, namely, division of the pain tract. One of the patients had been no better for that procedure, the other much worse.

Mr. R. C. ELMSLIE said that like Mr. Muirhead Little, he was personally unrepentant concerning the Syme amputation. He regarded a good Syme as a good amputation, though he knew that the limb-fitting was a difficulty, particularly if the limb was not kept in perfect order and if the fitting was not perfect, for, sooner or later, there was liable to be trouble with the stump.

There was another amputation which he—and perhaps others too—would condemn, namely, amputations through the knee-joint. Yet he had amputated through the knee-joint on three occasions in recent years. In each of those three cases, however, he was amputating for a congenital deformity in which the tibia was missing, and these children had been, all their lives, accustomed to get about on the flexed knee, so they had absolutely perfect end-bearing on the condyles of the femur, and by amputation through the knee-joint this end-bearing was retained. One of these operations had been performed ten years ago. Therefore, though one could condemn a form of amputation generally, one might encounter special circumstances in which such an amputation was indicated.

He had had two or three cases of children with congenital deformities of the feet, who had had a Syme amputation, in which the Syme end was tapering and not bulbous so that it would fit into a tapering bucket like an ordinary below-knee bucket, with perfect end-bearing in what was otherwise a below-knee stump. It was a Syme amputation which left conditions like those of an ordinary stump, and which had end-bearing in addition. The mind must always be open as to the best means of dealing with special cases.

Mr. ROWLEY BRISTOW said he agreed with the President, that one occasionally came across a Syme's amputation stump which lasted well, and was satisfactory. More often a Syme stump, although satisfactory for a year or two, gave trouble later. He had recently reamputated in a case of a woman who had had a double Syme seven years before. The stumps had remained good for about five years. One was moderately good from the first, and the other would have been passed as a very good Syme, which fulfilled all the requirements of an amputation stump. Between the fifth and seventh year the end had become "wobbly" and began to give trouble.

Another point of interest was the question of the treatment of the nerve-end. He agreed with the President that it was the small nerves which were the cause of the trouble, e.g., the internal saphenous in the leg and the internal cutaneous in the arm. Even in civil practice it was worth while to shorten those nerves, to crush them and perhaps to put a ligature round them.

Mr. A. ROCYN JONES said that when he had been assistant to Mr. Muirhead Little he thought that gentleman invariably injected the nerves with alcohol, and he himself believed that to be a valuable course to adopt in emergency amputations, namely, when one had to do a primary amputation—perhaps through a bad fracture, to diminish shock.

He was interested to hear Mr. Verrall say he did not drag on the nerves; that was the old custom. He quite appreciated the point that there were some small fibroses, and it was important to recognize that these might contribute to the tenderness of the areas one met with after these amputations.

Mr. S. L. HIGGS said that, at Roehampton, when he spent a longer time in getting the wound absolutely dry, and then stitched the wound up with interrupted stitches, not with a continuous suture, the bogie of hæmatoma formation was disposed of. He strongly advised surgeons never to put in a drainage tube, except in special circumstances.

Mr. BRISTOW (in response to a request by the President) said that the first arthroplasties of the hip which he had performed were in amputation cases. The operation was simpler to carry out with an amputation stump than with the whole limb.

One case he particularly remembered, in 1918 or thereabout, was that of an officer who had double ankylosis of the hip with severe flexion and abduction deformity and two short thigh stumps. That patient, after arthroplasty, was fitted with limbs, drove his small car, and walked quite reasonably well.

The PRESIDENT (in reply) said that Mr. Elmslie, whose opinion he had particularly wanted to hear on the Syme operation, said the Syme was good. That was not denied at all. He had himself seen many good Symes, and, as Mr. Elmslie said, much depended on good limb-fitting; but one saw so many cases that one had to legislate for the greater number. His own experience brought him to the conclusion that, legislating for the greater number it should be taught that the chance was against a permanently satisfactory position with the Syme. He was much interested in the Syme with end-bearing which resembled a mid-tibial. It must have been exceptional because of its good circulation; one would have expected the circulation to be bad.

Mr. Elmslie had referred to amputations through the knee-joint in cases of congenital deformity. He (the President) remembered one such case of Mr. Elmslie's and there was no question that it was a good amputation. He did not condemn the through-knee amputation from the surgical point of view; he merely said it was a bad amputation from the point of view of the clumsiness of its limb-fitting.

As to crushing of nerves and shortening: crushing he believed in, pulling down and shortening he did not. Whether the injury was in civil life or as a result of war wounds, less and less often did he pull down those nerves, as he was sure that the procedure caused peri-neural fibrosis.

He was puzzled by Mr. Rocyn Jones' reference to injecting nerves with alcohol in emergency operations. It was probably a good suggestion, but he did not like to stray into other tissues, beyond the area of damage, even with a hypodermic needle.

Section of Surgery.

President—Mr. C. H. FAGGE, M.S.

[*November* 5, 1930.]

PRESIDENT'S ADDRESS.

Aims and Limitations of Modern Surgery.

By C. H. FAGGE, M.S.

No one can have had charge of patients for thirty years as I have had, without from time to time contemplating his results. Have his ideals been achieved? Have his aims been fulfilled? "Who aims at sky far higher shoots, than he who means a tree," must make a strong appeal to us all.

He is a happy man who after many years of surgery can truthfully claim—and no doubt many will make such a claim—that his aims are still to the infinities of the heavens.

But the philosophic surgeon will admit that his ideal has never been accomplished. His ideal was, as it still is, the restoration to the normal, both of organism and tissue, and surgery, in spite of continued advance, has never reached this level.

It is to be deplored that so much of our time is taken up and that our energies both mental and bodily are expended in attempts to prolong life in patients suffering from terminal states, for whom our best endeavours can do no more than leave them in a condition far short of normal; in truth, far too much of modern surgery is mutilation. Admittedly in the present state of our knowledge it cannot be otherwise, but this does not prevent us from dreaming of more perfect surgical ideals. It is unnecessary to quote examples, for any operation list of a hospital staff's day's work provides many; in fact, if we exclude the correction of some injuries, such as fractures, and cosmetic operations, such as those for congenital deformities, e.g., cleft palate and hare-lip, there is little in our technique which does not replace one evil by another, admittedly of less, and usually of an unimportant degree.

That fascinating branch of surgery which endeavours to combat the ravages of age by transplantation of an organ or part of it from an ape closely allied to man, or to replace a damaged or diseased organ by a similar organ taken from another human, or to fill in a deficiency such as an absent finger by grafting another in its place, is still in its infancy. The laws which make for success are beginning to be understood and it is clear that much that has been exploited cannot bear the scrutiny of judgment by results. In fact, we may assert that the grafting of an organ or part of an organ from an animal is only of temporary benefit and that transplantation of an organ from man to man can only be successful when the technique of connecting the blood-vessels of the transplanted viscus to those of the recipient has been improved to a degree not yet possible, so that immediate restoration of the necessary nutritive fluids can be established with a reasonable degree of certainty. This restoration of circulation applies not only to blood-vessels, but also to lymphatics; in fact, the former may be satisfactory and the latter imperfect, as is seen in the tendency to a solid œdema shown by tubed and other bulky skin grafts, which persists for months when their vitality is not in question.

Let us now pass to a consideration of the physical limitations by which our work is hemmed in. I propose to exclude all those which are engendered by the morbid states of our patients and only to deal with limitations which result from the nature of bodily tissues and from the healing of every operation wound.

There is some truth in a remark which Lord Moynihan made at a recent Hunterian dinner to the effect that surgery as a craft had reached finality—a statement which the late Lord Birkenhead attacked with all his dialectic skill. It is probably unnecessary to remind the more senior of my audience that this idea is not new; in fact, in an American journal I recently came across a quotation from Erichsen to the same effect, made at the time when Listerism had become firmly established. But if the half truth be admitted, so must the reservation that even with our very best technique, the finest and most accurate primary union results in the formation of a scar.

In this relation the work of Aymard [1] may be recalled: he endeavoured to reduce the width of scar to its smallest possible dimensions by cutting the skin very obliquely and replacing and suturing the flap with meticulous care.

It is obvious that a width of scar, which is of no importance in the coarser tissues, is an absolute bar to function in the more highly specialized glands, and completely blocks the transmission of impulses in any part of the nervous system, either central or peripheral.

Modern aseptic technique has undoubtedly modified the amount of scar formed in any tissue operated upon, by limiting the leucocytic infiltration, but it is generally believed that proliferation of the fixed connective tissue cells is the ultimate factor in the causation of fibrous tissue and, so far as I know, there is no means by which this may be controlled.

But my first object in directing attention to scar tissue was an endeavour to decide what happens to any one of the higher connective tissues when it is subjected to an abnormal strain. To anyone who has operated on a patient who has already undergone a radical cure for inguinal hernia of the Bassini type, the appearance of the conjoined tendon will be familiar. In normal conditions this forms a robust muscular upper border to the inguinal canal, which by its contraction is closed at the upper end, so forming a perfect sphincter to the internal abdominal ring when the muscles of the abdominal wall are put into action. Now when the conjoined tendon is sutured down to the inguinal ligament, one of two results ensues: either the stitches cut out, or the somewhat bulky mass of muscle degenerates and becomes converted into a comparatively thin fibrous barrier. As such it may provide a sufficient protection against recurrence, but its function is now merely mechanical, and its structure is grossly altered. I cannot believe that my observations on several such results are exceptional, and I would like to hear from other speakers whether they have come to similar conclusions or not.

What I have just said only provides an example of a surgical principle of which the truth must be admitted, i.e., that human tissues dislike abnormal tension. When applied to the soft parts, a strain, in my judgment, usually results in a suture material of whatever nature or strength, cutting through, with a giving way of the structure which it is desired to hold down, or in the formation of scar by degeneration of the tissue held down. This limitation appears to me to apply to so many of the operations described under the name of *pexies*, and a particular example which illustrates my point is that of orchidopexy.

Consideration of this behaviour of soft parts under strain brings me to another type of technique—operations for incisional or ventral hernia. Here an area of scar has been produced by infection, and the fibrous tissue over this area offers a feeble resistance to normal abdominal tension. The normal resilient elastic abdominal wall has been replaced by an inelastic scar; we speak of this as stretching, but as a fact it gives way and a gap results. Our object is to replace the scar by normal resilient muscular layers. Many operations have been devised and much ingenuity has been expended in attempting to close this defect, and yet the majority of such devices can only replace a thin weak scar by a thicker, more resistant one. Such is the method of action, in my opinion, of metal filigrees, or of the introduction of living suture material—fascia lata,—after the method of Gallie and le Mesurier [2].

I submit that in dealing with such cases we should concentrate our attention not on the gap but on the tissue which fills it; thus let us begin by a free excision of all abnormal fibrous tissue, i.e. scar, and let me here point out that one's heart must be hardened and one's courage steeled, for often a most alarming gap will be left. When this has been done, normal aponeurotic and muscular layers can be approximated severally, and it is all-important to spend time in accurately defining the layers of the abdominal wall and suturing them one by one. I have not so far met with any incisional or ventral hernia which I could not close in this way with ordinary catgut sutures, though I will admit that I was once carefully scrutinized by two old dressers who thought that I had made so big a gap that I could never close it. My former Registrar, Mr. Eckoff, lately set up an inquiry with regard to patients dealt with in this way, and while the number is too small to provide any statistical conclusions, it is interesting to note that no recurrence was revealed and they were all following their normal occupations without pain or the use of any appliances.

A most interesting eccentricity of scar formation is traumatic keloid. I remember about thirty years ago observing that after an operation for inguinal hernia in small children, if the incision encroached on the hair-bearing pubes, that part of the scar might be keloid, and the rest a thin normal scar: I have now a patient operated upon recently whose cholecystectomy scar is keloid above and below but normal in the middle. It is my belief that a keloid, if excised freely, may not re-form.

With this I shall leave the subject, the thesis of which seems to me to be the limitations imposed upon our work by the nature of the bodily tissues and by the pathological formation of scar tissue, and an endeavour to determine how scar may be avoided and, if present, how it should be dealt with.

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Discussion.—Mr. C. MAX PAGE said Mr. Fagge had suggested that surgical operations with the exception of face-lifting and similar procedures were mutilating. Yet the President himself, later on, had dealt with operations for the relief of hernia in which, surely, there was restoration to the normal, or nearly so. Bone-grafting, again, could be placed in the same category, though admittedly this was not often performed.

His own treatment of certain ventral hernias differed from that advocated by Mr. Fagge. In cases in which there was a large gap he had usually performed a plastic operation, generally without the use of any foreign material. He had endeavoured to get apposition of the main bulk of the abdominal wall by overlapping, as in the Mayo operation for umbilical hernia, and he considered that his results were good. He had, however, no strong views on the subject. In the Mayo "double-breasted waistcoat" operation no attempt was made to suture the various layers of the abdominal wall in detail, yet good results ensued, and he did not see why this method should not be adopted in cases of incisional hernia.

He had been interested to hear the President say that keloids could be excised and a sound scar secured. He (the speaker) had thought that if one excised a keloid, another came in its place; but that might be because he had not tried it.

Mr. ZACHARY COPE said that the limitations of surgery might be dealt with from several points of view. One could take, for example, the limitations enforced by a multiplication of specialities. There was a tendency for the individual surgeon to become restricted to one small sphere, and if specialities continued to increase at the present rate, one could not say within what limits the individual surgeon might not ultimately be confined.

Strictly speaking, there could be no limitation to surgery; if it was to live it must advance. There might be limitations in some directions, but it would be found that there were other paths by which the surgeon could advance. The first time that the statement about surgical limitations was made (by Erichsen, fifty years previously) the kidney, the brain, and the spinal cord had not been operated upon, and most of the internal viscera had not been touched. Now, however, it could be said that every viscus, from the pituitary body to the depths of the spinal cord, had been dealt with. The advance of the future would, he thought, be in the direction

of a greater and more intelligent co-operation of the surgeon with the physician; there would some day be an end to the present occasional opposition between them. He did not see why, in the next ten years, there should not be discovered a real medical cure for exophthalmic goitre, as that condition must be due to a toxic process. Occasionally sudden changes occurred in it without operation, and infection sometimes played a part. There should also be a method of curing gastric ulcer without operation.

The President had said that it was impossible to make a cut without getting some form of scar. There was a way of extirpating disease which left no scar worth mentioning, as in the tongue, namely by radium treatment. The tissue left after such application was practically normal in appearance. Might it not therefore be that in the application of radium therapy there would be in future the disappearance of scars and the re-appearance of normal tissue? Many keloids would vanish under X-ray treatment; they certainly became softer. It was reasonable to look forward to the time when, by some modification either of length of application or of actual rays, scars might be banished, and normal tissue appear.

Mr. A. J. WALTON said that as the surgeon grew older he asked himself what was being done in surgery. He felt more and more, on contemplating results, that the aims of the surgeon in the future would be to abolish surgery. Practically everything done by the surgeon was a mutilating operation. He, personally, had always laid down the law that in surgery as little as possible normal tissue should be removed.

Mr. Cope had raised two interesting questions, which had always been present in his (the speaker's) mind. One was that surgical operation for exophthalmic goitre was theoretically wrong, but it was at present the only certain method of cure. Still, one could not envisage surgery going on for many years and being still associated with such mutilating operations.

The second point was one of gastric surgery. He thought that the Continental method of removing half the stomach on account of a small ulcer was, theoretically, wrong, and he could imagine that in the future all such operations would be abolished. He was finding, in his own practice, that he was doing more medicine and less surgery.

The most ideal surgical operations—those which aimed most directly at the restoration of normal function and anatomy—were those for the removal of benign tumours; next came those for restoration after accident. And Mr. Max Page had mentioned fractures; these were wounds of normal tissue, operations for which did restore very nearly the normal condition with a minimal formation of scar tissue.

In regard to the treatment of ventral hernia, his experience supported what the President had said. He (Mr. Walton) had never felt convinced as to the value of the filigree operation. By carefully dissecting, and treating the layers one by one, the surgeon achieved success. There was, however, an exception, namely, when the hernia had arisen owing to pronounced nerve destruction. He knew no condition so hopeless as [illegible] which there was paralysis of the rectus muscle or of oblique muscles. In those cases [illegible]ation was almost impossible. But, for the rest, he agreed with the removal of scar tissue.

Mr. W. E. TANNER asked if the President approached those median supra-umbilical hernia cases in which there was the barrel-shaped chest with bronchitis, with the same certainty that he approached the ordinary case of incisional hernia.

Mr. E. I. LLOYD asked if Mr. Fagge's philosophy could explain the curious variations of keloid in patients suffering from various congenital deformities, particularly children who had just escaped having a hare-lip. Probably all surgeons had seen such patients with scars which Nature had produced, of a kind which the surgeon tried in vain to emulate. Why did Nature do this in such a superior way? One could take this point a stage further. One had only to remind oneself of the development of the face to realize that every face was made up of a series of marvellously sutured seams.

With regard to keloid, he had been impressed in his own small experience with the occasional occurrence of keloid at the lower end of the inguinal incision, and he believed that it occurred more frequently in the lower end of the hernial scar than in the upper. But whether, as the President suggested, that was due to its encroaching on the pubic hair was matter for conjecture. His own work was largely among children, who had as yet no pubic hair. His experience suggested, especially in connection with undescended testes, that the lower the wound, the more liable was it to show keloid. He had excised keloids and seen them recur. He thought the proper treatment was not to apply X-rays or radium immediately, but to excise the keloid and then apply radium. Some patients appeared to be

more liable to keloid formation than others. Many children whom he saw seemed particularly liable to it.

When one thought of some patients, particularly, perhaps, those with burns or scalds, one wondered how far the efforts to correct these deformities and disfigurements had produced a cure almost worse than the disease. In one patient he (the speaker) had carried out a successful pedicle graft, but was horrified a few months later to find that the abdominal wall from which the pedicle had been taken presented a large mass of keloid ¼ in. in diameter, though at the operation the suturing had been accurate and sepsis had been absent.

The PRESIDENT (in reply) said that he had not meant to imply that every incisional hernia could be cured in the manner described. He meant that he had not so far met with any incisional hernia which he could not close in that way.

In many ways it was important to find out the limitations of one's surgical capacity, and every surgeon should confine himself to those methods which he could use satisfactorily. He did not doubt that Mr. Max Page could cure incisional hernias by the method which he employed, and if he found that to be a satisfactory method, it was surely better to continue to use it than to embark on something which someone else advocated.

He could express no opinion on the question asked by Mr. Lloyd, as to the scars occurring on the face in newly-born children.

In reply to Mr. Walton, he (Mr. Fagge) had been fortunate in never having had to deal with a hernia due to paralysed nerves, nor had he dealt with a case of the kind mentioned by Mr. Tanner, but in bad subjects with abdominal hernia he had managed to get along satisfactorily under spinal anæsthesia.

He admitted that his explanation of keloid in the lower end of hernial scars was pure theory; the suggestion that keloid formation might be due to the influence of sebaceous glands might not bear scrutiny. It used to be said, though he had never seen anything to support the view, that keloid indicated a tuberculous tendency. It was his experience that a tendency to form keloids was much more pronounced in some patients than in others.

Section of Surgery.

SUB-SECTION OF PROCTOLOGY.

President—Mr. Lionel E. C. Norbury, F.R.C.S.

[*November* 12, 1930.]

PRESIDENT'S ADDRESS.

Multiple Primary Malignant Growths. With Special Reference to the Colon and Rectum.

By Lionel E. C. Norbury, F.R.C.S.

It has often been remarked that proctology is such a small branch of surgery, and that disorders of the rectum and colon have been so fully dealt with at previous meetings of this Sub-Section, that little remains for future discussion and Presidential addresses.

I would like to remind those whose thoughts run in such narrow channels that carcinoma of the rectum accounts for more than one-third of all malignant growths of the alimentary tract, and that this subject alone gives food for much research and thought. At our last meeting, Sir Charles Gordon-Watson read a valuable paper on the treatment by radium in this connection.

The subject of this present address is "Multiple Primary Malignant Growths, with special reference to those occurring in the Rectum and Colon." I was led to the choice of this subject by having had under my care:—

(1) Two cases of the simultaneous occurrence of carcinoma in the breast and rectum;

(2) A case of bilateral and simultaneous primary carcinoma of the breast, followed at a later date by rodent ulcer of the nose;

(3) A case of carcinoma of the breast followed some fifteen years later by carcinoma of the opposite breast;

(4) A patient upon whom I operated for acute intestinal obstruction, who exhibited three primary carcinomata—one in the rectum—a second in the pelvic colon and a third in the transverse colon;

(5) A patient with carcinoma of the colon following perineal excision of the rectum for carcinoma six years previously;

(6) A case of two simultaneous carcinomatous growths in the rectum.

On looking up the literature, I find that multiple primary malignant growths are by no means so uncommon as is usually supposed, in fact there are many such cases recorded: It may seem that one is overstepping the boundaries of proctology by a consideration of multiple tumours in other parts of the body. Proctology is not, however, a water-tight compartment—and certain points of interest and practical importance I think may be gained by such a study. I wish, however, to refer especially to multiple primary malignant growths of the large bowel and rectum.

Multiple primary growths in general.—The presence of multiple tumours occurring in the same individual has been recognized for years. With certain growths, the tumour formation was found to be more often multiple than single.

Virchow called attention to the presence of multiple fibromata of the skin, as also did von Recklinghausen. These two observers noted moreover that such tumours sometimes underwent malignant changes and were transformed into sarcomata. Later, similar cases were reported by others.

The presence of *multiple malignant tumours* is, however, not so common, although more common than is usually believed. Wells [1] in 1901 collected 17 cases of multiple primary tumours and three cases of the so-called "carcinoma sarcomatodes." Wooley [2] in 1903 collected 26 examples of multiple primary carcinomata, five of multiple primary sarcomata and four of multiple malignant growths of more than one type; Theilhaber and Edelberg [3] in 1912 collected 44 examples of multiple primary carcinomata in the same system of organs and 41 cases in various organs; Bartlett [4] in 1914 reviewed 95 cases of multiple primary tumours; Reichmann in 711 post-mortems found two examples; Redlich [5] in 507 post-mortems also found two examples, and Goetting [6] in 1,000 necropsies discovered a similar number. Major [7] records a case of carcinoma of the face and round-celled sarcoma of the stomach occurring in the same individual. He deals exhaustively with the literature on the subject and reviews 628 examples of multiple primary malignant tumours. 389 were examples of multiple carcinomata in the skin—in the same organ or in each of a pair of organs. Tabulation of "Carcinomata in different organs but belonging to the same system" shows 43 examples.

"Carcinomata in various organs" (not the same system) shows 53 examples.

123 instances of different types of tumour in the same person were recorded:—In 66 the tumours were in the same organ; in 9 they were in organs belonging to the same system; in 48 the different tumours were located in various organs.

The most common combination of different types of malignant tumours was that of carcinoma and sarcoma. The presence of both carcinoma and sarcoma in the same organ has led to much discussion, especially since the work of Virchow who laid stress upon the carcinoma sarcomatodes or tumour in which both elements were present.

Examination of the literature shows that co-existing malignant growths are not so uncommon as is often supposed.

Offergeld [8] reports a case of bilateral primary sarcoma of the breast, also one of bilateral primary breast carcinoma, and a third case of simultaneous carcinoma of breast and adeno-carcinoma of the uterus. Harrington [9] describes a case of carcinoma of breast removed by operation and followed 25 years later by a similar growth in the opposite breast. Riley-Russum and Barry [10] mention the occurrence of simultaneous and independent carcinomata of the breast and stomach. Orr [11] in a recent article records three cases of multiple malignant growths occurring at St. Mary's Hospital:—(1) A case of squamous-celled carcinoma of tongue, with columnar-celled carcinoma of the stomach, arising in a peptic ulcer in a male, aged 62 years. (2) Male, aged 71. Columnar-celled carcinoma of stomach, combined with columnar-celled carcinoma of the rectum. No metastases found in other organs. (3) Female, aged 67. Scirrhous carcinoma of breast co-existing with columnar-celled carcinoma of the colon.

Siebke [12] in 1926 collected 53 instances of multiple carcinoma from the literature and reported two cases in which carcinoma of the stomach was combined with carcinoma of the cervix and body of the uterus.

My own cases presented certain interesting features:—

(I) Female, aged 45. Tumour in both right and left breasts. Enlarged axillary glands. Radical operation on right breast, followed nineteen days later by similar operation for left breast. *Microscopy*: Encephaloid carcinoma of both breasts and also axillary glands of both sides.

X-ray treatment followed. No sign of recurrence up to the present, i.e., 8½ years after operation. Rodent ulcer of nose of some two years' duration, recently excised.

(II) Female, aged 70. Radical amputation of left breast for carcinoma 15 years previously elsewhere. *Microscopy*: "Scirrhous carcinoma—glands unaffected." Tumour, right breast, noticed for 18 months. Growth fixed, ulcerating; hard axillary glands.

Treated with Radium.

(III) Female. Extensive scirrhous carcinoma of breast—treated by radical operation. Patient complained of diarrhœa at the same time, but no notice was taken of this until after removal of the breast. Digital examination a few weeks later revealed an extensive carcinoma of the rectum, necessitating colostomy at a subsequent date.

(IV) Female, aged 57. Carcinoma of rectum and recto-vaginal septum five years ago. Treated with radium and subsequent colostomy, with further insertion of radium.

Carcinoma of right breast two years after lesion of rectum was first noticed: successfully treated with radium.

I would also mention the case of a woman, aged 80 years.

The left breast was removed on account of carcinoma twenty years ago. No local recurrence in scar or glands. A malignant growth appeared in the *right* breast nine months ago. This is without doubt a second primary lesion. Three other cases will be mentioned when considering multiple growths of the rectum and colon.

Roy Ward [13] in an article on "Radium Treatment for Rodent Ulcer, etc.," states that "Multiple lesions are more common than is usually supposed." In his series of cases there were 94 instances—55 in men and 39 in women. In one case, that of a woman, aged 28, nineteen different lesions were treated with radium. Ward also emphasizes the fact that a rodent ulcer may take on the characteristics of a squamous-celled carcinoma. Forty such cases occurred in his series.

Contributory factors in the development of multiple malignant neoplasms.—It has long been a disputed point as to whether one malignant growth has an inhibitory influence on the development of a second. Experimental work in animals of transplanting portions of an autogenous malignant neoplasm to healthy tissue in another portion of the body, has shown that the primary malignant growth tends to disappear. This would suggest an inhibitory influence, the result of the development of antibodies. One might suppose, therefore, that the presence of one malignant growth would afford some degree of immunity or protection against the development of other primary lesions.

Major [7] in his summary of cases of multiple malignant tumours states that no single explanation suffices to explain the incidence of multiple primary malignant tumours in all cases. Coincidence may account for some, but deeper causes are at work in others. He considers that in dealing with the ætiology of multiple primary growths two factors are probably at work: (1) Transmission by infection and (2) the multiple origin of tumours.

(1) "Contact may spread a carcinoma from a primary growth to an adjacent organ, e.g., skin of scrotum to the thigh; one labium to the opposite side; one lip to another.

(2) The multiple origin of carcinomata is, however, a well-established fact. Petersen [14] and Hauser [15] have shown that carcinomata may arise simultaneously from several centres, e.g., in polyposis of the stomach and intestine. (This will be referred to later.)

The presence of different types of tumour in the same organ, e.g., carcinoma and sarcoma, may or may not be a coincidence. Erhlich and Apolant [16] by repeated inoculation of a typical adeno-carcinoma in mice succeeded in changing it first into a mixed tumour and later into a typical sarcoma.

Russell [17] has recorded the case of an adeno-carcinoma of the breast in a mouse which, after continuous growth in the animal, gradually became sarcomatous and at a later date a pure sarcoma. This change seemed to be controlled by the time element, since early transplanted portions produced a carcinoma, whereas if allowed to grow until it became a sarcoma, inoculated animals developed a

sarcoma. Such experimental findings suggest the presence of some abnormal stimulus, which acts on both epithelial and mesodermal elements, producing either epithelial or mesodermal tumours, or a combination of the two. Kidner [18] reports a case in which removal of a sarcoma was followed later by the appearance of a carcinoma at the site of the old operation.

Major's statistics show that multiple malignant neoplasms have no predilection for organs of the same system, excluding paired organs, e.g., the ovaries. Multiple primary tumours appear to be more common in organs not related by any system. The occurrence of multiple tumours in various organs must be more than a coincidence. The susceptibility of individuals of certain families to malignant tumours is a well-known clinical observation. This is substantiated by the breeding experiments of Slye who has shown that mice, with a cancerous ancestry, have a marked tendency to develop spontaneous cancer, and that such mice develop carcinoma as the result of trauma which, in control animals of non-cancerous ancestry, produces no result. It would appear, therefore that individuals developing multiple malignant tumours have some sort of susceptibility to tumours which is not limited to any one organ or region of the body. The occurrence of two or more distinct malignant growths may be explained therefore by predisposition, and that subsequent irritation in the affected organs results in the production of malignant neoplasms.

In Major's statistics there are nine examples of three primary tumours and two examples of four primary tumours occurring simultaneously. Lewis [19] reports nine different tumours in the same patient and Sliwinsky [20] seven. Cuthbert Dukes [21] remarks that the incidence of multiple malignant tumours has an important bearing on the pathology of cancer, since an accurate record of frequency may decide the disputed problem as to whether one malignant growth exercises an inhibitory effect on the development of a second.

He quotes Orr's figures from St. Mary's Hospital statistics and states that these and other published records are not sufficient to settle the question definitely or to warrant the conclusion that the presence of one malignant tumour exercises any influence on the development of a second.

Multiple primary malignant growths of the rectum and colon.—The occurrence of multiple neoplasms in the large bowel has been recognized for some time past. The fact that they are separate primary lesions is a more recent observation. The multiplicity of such growths in the first instance was explained by the engrafting of detached fragments from a primary lesion on to portions of mucous membrane above and below. In other words the process was regarded as one of infection or contact. Maingot [22] describes the case of a woman, aged 46, whose rectum was excised, 19 in. of bowel being removed. The specimen showed a carcinoma in the ampulla of the rectum, a second in the sigmoid colon, and a third in the anal canal. Sections of all showed "adeno-carcinoma." The growth in the rectum was regarded as primary and those in the anal canal and sigmoid colon as "contact" or "kiss cancers" from the primary lesion. No mention was made in this case of the presence or otherwise of polyposis.

Although a number of cases of multiple primary neoplasms of the *large bowel* have been recorded, the incidence is not so great as that of multiple growths arising simultaneously in various organs of the body, already considered. In Major's large series of 628 cases the following occur:—

(*A*) Carcinomatous growths, co-existing in the same system of organs: jejunum and colon, 1; stomach and colon, 2; stomach and rectum, 3; larynx, stomach and rectum, 1; œsophagus and colon, 1.

(*B*) Growths arising simultaneously in various organs: (*a*) Lips, hands and cæcum; (*b*) uterus and colon; (*c*) lip and rectum; (*d*) gall-bladder and rectum; (*e*) eyelid and rectum; (*f*) bladder and anus; (*g*) ovary and colon; (*h*) breast and colon; (*i*) skin of buttocks and rectum.

(*C*) Different tumours arising in the same organ (namely carcinomata and sarcomata): Such co-existing tumours were found to occur chiefly in the uterus, breast and thyroid. No such cases were recorded in the rectum or colon.

(*D*) Different tumours arising in the same system of organs: None recorded in the rectum or colon.

(*E*) Different types of tumours in various organs: One case of carcinoma of the uterus arising simultaneously with melanotic carcinoma of the rectum.

I intend to confine my remarks principally to multiple primary malignant neoplasms of the rectum and colon. I have had four such cases under my care recently:—

(I) Male, aged 76, with symptoms of acute intestinal obstruction. A finger in the rectum detected an extensive malignant growth. A left iliac colostomy was decided upon. On delivering the pelvic colon, a second malignant growth was discovered, narrowing the sigmoid loop considerably. Examination of the transverse colon revealed the presence of a third neoplasm. A transverse colostomy above the uppermost growth was therefore performed, and relief of symptoms followed. There was also evidence of diverticulosis of the pelvic colon. Unless the pelvic colon growth had presented in the wound, a sigmoid colostomy might easily have been performed with the erroneous idea that the colostomy was well above the site of obstruction.

(II) Female, aged 66. Removal of rectal polyp by a colleague in 1924. Microscopy showed evidence of carcinoma. Subsequently colostomy and perinæal excision of the rectum were performed. 1929, Frequent passage of blood and mucus from the colostomy. Abdominal exploration: Transverse colon incised and a small simple polypus removed. Symptoms still persisted. Digital examination through the colostomy revealed small irregularities of the mucous membrane, probably multiple small polypi. In July, 1930, a portion of polypoid tissue was passed per colostomy. Microscopically, the histological features were those of a papilliferous columnar-celled carcinoma. The tissue examined was probably a portion of a larger growth. This case was without doubt one of "multiple adenomata" with subsequent malignant transformation of certain polypi, a pathological condition which will be referred to later.

(III) Female, aged 62. Colostomy and perineal excision of rectum, January, 1930.

Pathological report.—"An ulcerated columnar-celled carcinoma of the rectum. There is a second small malignant papilloma present a short distance below the former. No metastases present in the glands."

(IV) Female, aged 61. On digital examination a polyp was felt low down in rectum, as also an annular malignant stricture in the pelvi-rectal region.

Polyp removed. *Microscopy*: "carcinoma."

The records of certain of the larger London hospitals contain very few instances of multiple malignant growths. Statistics kindly supplied to me from these sources show the following:—*St. Bartholomew's Hospital*: Only one case of multiple malignant growths recorded, although there were several cases of single growths associated with multiple polypi.

The patient was a male, aged 60, who was operated upon for acute intestinal obstruction. One growth was present 3½ in. from the anus, and a second growth 6 in. higher up the bowel, forming an annular stricture and probably the older growth. A colostomy was performed proximal to the upper growth.

King's College Hospital.—There was no record of any case of multiple malignant growths of the large bowel. Notes of a specimen of carcinoma of the sigmoid colon showing a solitary polyp higher up the bowel were, however, given to me.

St. Thomas's Hospital records showed the following cases:—

(I) Female, aged 50. "Carcinoma of the transverse colon co-existing with carcinoma of the cæcum."

(II) Female, aged 66. "Combined carcinoma of the rectum and sigmoid colon."

(III) Male, aged 27. "Multiple malignant polypi from cæcum to rectum."

(IV) Male, aged 75. "A large malignant ulcer at the ano-rectal junction associated with a similar smaller ulcer 5 in. higher up the bowel.

There was also a case of carcinoma of the splenic flexure associated with multiple polypi of the large bowel.

There have been several cases at St. Mark's Hospital under the care of my colleagues, who have kindly allowed me to have drawings made of the specimens removed, and to show them to you this evening. Abel [23] records a case of "Double carcinoma of the pelvic colon and rectum, associated with polyposis of the colon and duodenum."

The patient was a male, aged 63, with symptoms of frequent attacks of diarrhœa. Rectal examination showed a large growth at the pelvi-rectal junction.

Colostomy was performed. A pelvic abscess subsequently developed and the patient died.

Post-mortem examination revealed the presence of two separate carcinomata, one at the pelvi-rectal junction, and the other and larger 1·5 cm. higher up, the two being separated by healthy mucous membrane. Multiple polypi were present throughout the extent of the colon. Three distinct papillomata were also present in the duodenum just distal to the pylorus.

Abel also mentions three other cases of double carcinomata of the colon and rectum.

(I) A male, aged 58, for whom Mr. Miles performed abdomino-perinæal excision of the rectum and pelvic colon. Two separate and distinct carcinomata were found, one in the middle of the pelvic colon and one in the upper part of the rectum. Microscopy showed that each tumour was a columnar-celled carcinoma, with widespread lymphatic infiltration.

(II) Male, aged 56. Cæcostomy performed for acute intestinal obstruction by Mr. Miles. At the time of the operation, two growths were detected, one in the descending colon and one in the pelvic colon. At a later date these portions of the bowel were removed. The specimen showed two separate carcinomatous strictures.

(III) Male, aged 59. On examination, a growth was detected on the posterior wall of the rectum just below the pelvi-rectal junction. Abel performed an abdomino-perinæal excision of the rectum, when two separate malignant masses were found, one about 4 in. above and the second just below the pelvi-rectal junction. Microscopy showed both growths to be columnar-celled carcinomata.

In none of these cases is any reference made to the presence or absence of multiple adenomata.

Ætiology of multiple growths of the large bowel.—With regard to the ætiology of multiple growths of the colon and rectum, certain pathological evidence is forthcoming. In an article on "The precancerous changes in the rectum and colon" by Lockhart-Mummery and Cuthbert Dukes [24] attention is drawn to the frequent association between multiple adenomata and carcinoma of the rectum and colon. The authors state that the earliest recognizable lesion in the development of cancer of the rectum is a hyperplastic change taking the form of irregular epithelial proliferations scattered over an extensive area of the bowel. This is followed by the appearance of visible tumours (adenomata), which are usually multiple and separated from each other by several inches of normal mucous membrane—the so-called "precancerous stage." At any period in the growth of the adenoma the epithelium may assume invasive properties, and the tumour become a carcinoma. Such a carcinoma may therefore be regarded in the light of an accident happening to a previously existing adenoma. If such malignant changes can arise in one adenoma it is not hard to imagine a similar transformation of a second or even of several adenomata. This is well illustrated in a specimen in the museum of St. Mark's Hospital, in which three separate malignant tumours are present, accompanied by adenomatosis. Beneath each malignant tumour the sub-mucosa is invaded by cancer cells, but the intervening tissues show no infiltration. It is a case of cancer supervening on adenomatosis, the malignant disease commencing in three separate places. In view of the precancerous nature of adenomata, it is essential that when discovered and when practicable, all such growths should be removed.

In the development of carcinoma of the rectum the following sequence of events can be noticed:—

(1) Localized patches of hyperplasia, invisible to the naked eye, and affecting an extensive area of the bowel.

(2) The appearance of a crop of sessile adenomata scattered over an area coinciding with the original area of hyperplasia.

(3) The development of cancer in one or more of these adenomata, or in the neighbouring epithelium.

(4) The progressive enlargement of the malignant tumour with retrogression of the hyperplasia and benign tumours surrounding the malignant growth.

Experiments on animals have proved that the onset of carcinoma is usually preceded by a precancerous condition of the epithelium. This is evidenced in the rectum by patches of hyperplasia of the mucous membrane and adenomatosis. Pathological changes may be arrested at this stage and retrogression of hyperplasia may occur. Experiments upon mice have proved that the common chain of events when painted with tar is: (*a*) hyperplasia, (*b*) papilloma, (*c*) epithelioma. The papilloma is the precancerous stage in experimental tar cancer and the adenoma in human rectal cancer.

Polyposis intestini and its relation to multiple malignant tumours of the bowel.—Polyposis intestini is a disease characterized by adenomatous proliferations of the intestinal mucous membrane. It has a definite familial tendency of the Mendelian type. The disease is transmitted by both males and females, and both males and females suffer from the disease. The inheritance can be traced through several generations. The tendency is, sooner or later, for carcinoma of the rectum or colon to develop.

Doering [25] in reviewing the causes of death in fifty cases of polyposis intestini found that out of thirty-six patients in whom the cause of death was ascertainable, twenty-one died from cancer of the bowel.

There can be no doubt from the observations of Lockhart-Mummery, Dukes, Jungling and others that polyposis intestini is an inheritable disease. These authors have worked out and published pedigrees of their cases, which definitely prove this assertion.

Doering's statistics show that polyposis intestini is a disease of adolescence, or early middle age.

The following is his review of forty cases :—

Ages (years)	Cases	Ages (years)	Cases
1 to 10	2	40 to 50	2
10 to 20	10	50 to 60	2
20 to 30	10	60 to 70	1
30 to 40	13		

The disease may therefore not manifest itself for some years. The table proves that polyposis intestini is not a congenital disease, and that what is inherited is a predisposition to tumour formation.

" Polyposis intestini must be distinguished from isolated polypi in children or adults, and from the multiple small adenomata which often surround early carcinoma of the rectum and colon." The nomenclature of multiple polypi of the large intestine is rather misleading. The term " polyposis intestini " should be reserved for the familial type of multiple polypi, a disease which is very liable to early malignant transformation. The condition of multiple polypi of other than familial origin may be described as adenomatosis of the large bowel, multiple adenomata or multiple papillomata. Both of these primary types must be distinguished from multiple polypi, secondary to inflammatory lesions of the bowel, e.g., those following chronic ulcerative colitis, dysentery, bilharzia, etc. The name " colitis polyposa," or pseudo-polyposis," is applied to this condition. There does not appear to be any special liability for malignant changes to supervene in such cases. Hullsiek [26], as also Erdmann and Morris [27], drew attention to two distinct

types of polyposis: Adult and acquired, which may be single or multiple: (2) Adolescent or congenital (multiple and disseminated). This is the condition known as "polyposis intestini." Hullsiek states that multiple polyposis is most common in childhood and youth, the average age in his series being 30·9 years, with over 65% occurring before 35 years. Males and females are about equally affected. There is a definite hereditary tendency.

The probability of malignant change is high—in his series 34·6%. The mortality is high, amounting to 47·2% under all forms of treatment. Symptoms usually persist for a long time before medical attention is sought.

Dukes [28], in an illuminating paper on "The Hereditary Factor in Polyposis intestini," lays stress on the fact that the polyposis intestini is a constitutional disease which runs in certain families who inherit a predisposition to the development of proliferation of intestinal mucous membrane.

Polyposis may affect the whole colon and rectum or only a portion of the large bowel. A similar condition may be present in the stomach and small intestine either alone or in association with polyposis of the large bowel. It is not difficult to understand the development of multiple malignant tumours in a disease, where the tendency to malignant transformation is such a marked feature. From what has been said there can be little doubt that polyposis intestini will account for the presence of multiple malignant growths in a certain proportion of cases.

Conclusions.

Conclusions to be drawn from a study of: (1) malignant growths in general; (2) growths of the rectum and colon in particular.

(1) *Malignant growth in general.*—(*a*) Several primary growths may be present at the same time in various parts of the body.

(*b*) The presence of one malignant growth does not of necessity confer immunity to the development of other malignant tumours.

(*c*) When planning a radical operation for carcinoma the possibility of another primary growth either in the same viscus or in another portion of the body must be borne in mind.

(2) *Malignant growths of the colon and rectum.*—(*a*) Multiple polypi are commonly associated with carcinoma of the large bowel. One or more of these may undergo malignant transformation producing multiple primary carcinomatous growths.

(*b*) It is a well-established fact that adenomata of the large intestine are peculiarly liable to undergo malignant changes. Although apparently innocent, these tumours often exhibit microscopical appearances suggesting a precancerous state. Such tumours should be removed whenever possible, and in any circumstance, cases of this nature should be kept under careful observation.

(*c*) Sigmoidoscopy should always be employed to exclude the possibility of adenomatosis, or the presence of an already established second malignant growth in the rectum or lower pelvic colon.

From an examination of the literature it is evident that in the majority of cases of multiple malignant growths of the large bowel, the lesions are situated for the most part in the rectum or pelvi-rectal region.

(*d*) Filling defects as shown by the X-rays, are useful in the diagnosis of polyposis intestini, and multiple malignant strictures of the large bowel.

(*e*) One cannot emphasize too strongly the possibility of the presence of multiple growths, when planning an operation for excision of the rectum or resection of the colon for malignant disease. As a routine I would advocate careful examination of the whole of the colon; through an adequate abdominal incision, as well as of the liver, glandular distribution, etc., in all such cases.

(*f*) The prognosis after operation for removal of a malignant growth of the colon

or rectum will largely depend on the presence or absence of multiple polypi of the bowel from which other primary malignant growths may arise.

(*g*) It is not uncommon after excision of the rectum or partial resection of the colon for malignant disease, for the patients to die within a few years. It is conceivable in these cases that other unsuspected primary growths may have developed in the interim.

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Discussion.—Mr. J. P. LOCKHART-MUMMERY said that his own contribution to the subject would be a brief account of nine cases taken from his own records in which a second primary tumour had developed. He considered such cases of particular interest.

I. Male, aged 37. Cancer of rectum removed; eighteen years later another primary growth developed 11 in. higher.

II. Female, aged 68. Epithelioma of anus removed; duct cancer of breast developed four years later.

III. Male, aged 53. Cancer of rectum; primary growth developed eight years later in colon.

IV. Female, aged 48. Cancer of rectum removed; developed duct cancer of breast five years later.

V. Female, aged 70. Cancer of sigmoid removed; malignant polypus developed five years later in rectum.

VI. Male, aged 56. Cancer of rectum removed. Patient died five and half years later from primary cancer of bronchus.

VII. Female, aged 60. Cancer of rectum removed; adenoma of the transverse colon developed seven years later.

VIII. Female, aged 63. Cancer of rectum removed; primary growth of stomach developed five years later.

IX. Male, aged 43. Cancer of rectum removed; primary growth in colon developed thirteen years later.

Mr. TURNER WARWICK said that even apart from skin tumours, in which multiple foci of origin were not uncommon, multiple primaries were not infrequently met with in the post-mortem room, and in any large hospital at least one case a year would be found. That they had not reached the museums was perhaps due to the fact that the pathologist did not regard them as rarities. Thus no specimens could be found in the Museum of the Royal College of Surgeons, although the authorities there had been kind enough to make a special search for the purpose of this discussion.

He personally knew pathologists who had become interested in this condition, and had begun by collecting their own cases. When they came to collecting them from the literature, they had found the list so immense that they had given up the idea.

He (the speaker) had a few specimens to show. The first was from a case of multiple adenomatosis of the colon, in which two widely separated malignant foci had developed. The second was a specimen of adeno-carcinoma of the colon obtained by operation on a woman who had previously had her breast removed for mammary cancer. The third case was that of a man aged 45, on whom an exploratory laparotomy was performed for tumour of the abdomen associated with pain. The condition proved to be inoperable, the bulk of the tumour being found to be retro-peritoneal. An enlarged gland removed for microscopical

examination showed the structure of lympho-sarcoma, in the middle of which was a small deposit of columnar carcinoma. The man died shortly afterwards, and was found to have a carcinoma of the stomach apparently related to an ulcer. The main tumour mass was, however, lymphosarcoma. Two pedunculated tumours showing this structure were found in the cæcum.

From the point of view of interest he showed a section of the multiple myeloma of plasma-celled type. In this type a multiple focal origin was the rule. In Ewing's tumours also a multiple focal origin was not uncommon.

Lastly he was showing two sections of the carcinoid tumour of the small intestine. The first section showed a tumour about the size of a haricot bean. It infiltrated the whole walls of the intestine. In this case there were three or four tumours about this size, a distance of from six to twelve inches of small bowel separating the nodules. The second was an example of a more advanced carcinoid tumour, showing deposits in a gland in the mesentery.

Less than thirty metastasing carcinoid tumours had been reported, but he thought it a commoner condition than this paucity of records would lead one to suppose.

The tumours were supposed by some writers to be basal-celled carcinomas, bearing the same relation to the ordinary adeno-carcinoma of the bowel as rodent ulcer did to epithelioma of the skin. The cells stained well with silver nitrate however, and were more generally regarded as being of neurogenic origin, and associated with the local intestinal nerve plexuses.

The carcinoid tumour was more frequently met with in the appendix than in the small intestine. It had been found in a Meckel's diverticulum. As far as he was aware it had never been found in the large intestine (apart from the appendix), but no one had ever made a serious search for it there.

Mr. C. NAUNTON MORGAN showed two specimens from the St. Bartholomew's Hospital museum of multiple primary new growths of the alimentary tract.

One of these was an œsophagus containing three distinct squamous-celled carcinomata and the other a large carcinoma of the sigmoid colon, in which there was also a more recent carcinoma of the ampulla of the rectum.

FIG. 1.—Carcinoma of pelvic colon and carcinoma of rectum with small adenomata below. Normal mucous membrane between growths. (Mr. Lockhart-Mummery's case.)

FIG. 2.—Carcinoma at recto-sigmoidal junction with villous papilloma of rectum. (St. Mark's Hospital Museum.)

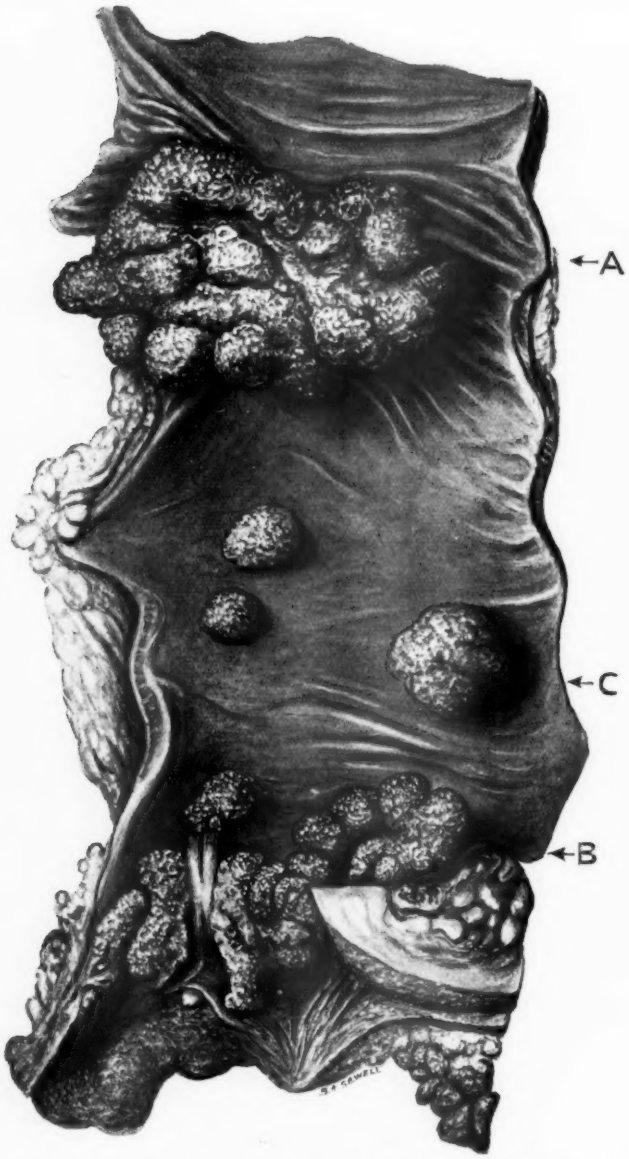

FIG. 3.—Multiple primary carcinomata of rectum and recto-sigmoidal junction. Normal mucous membrane between growths. (Mr. Lockhart-Mummery's case.)

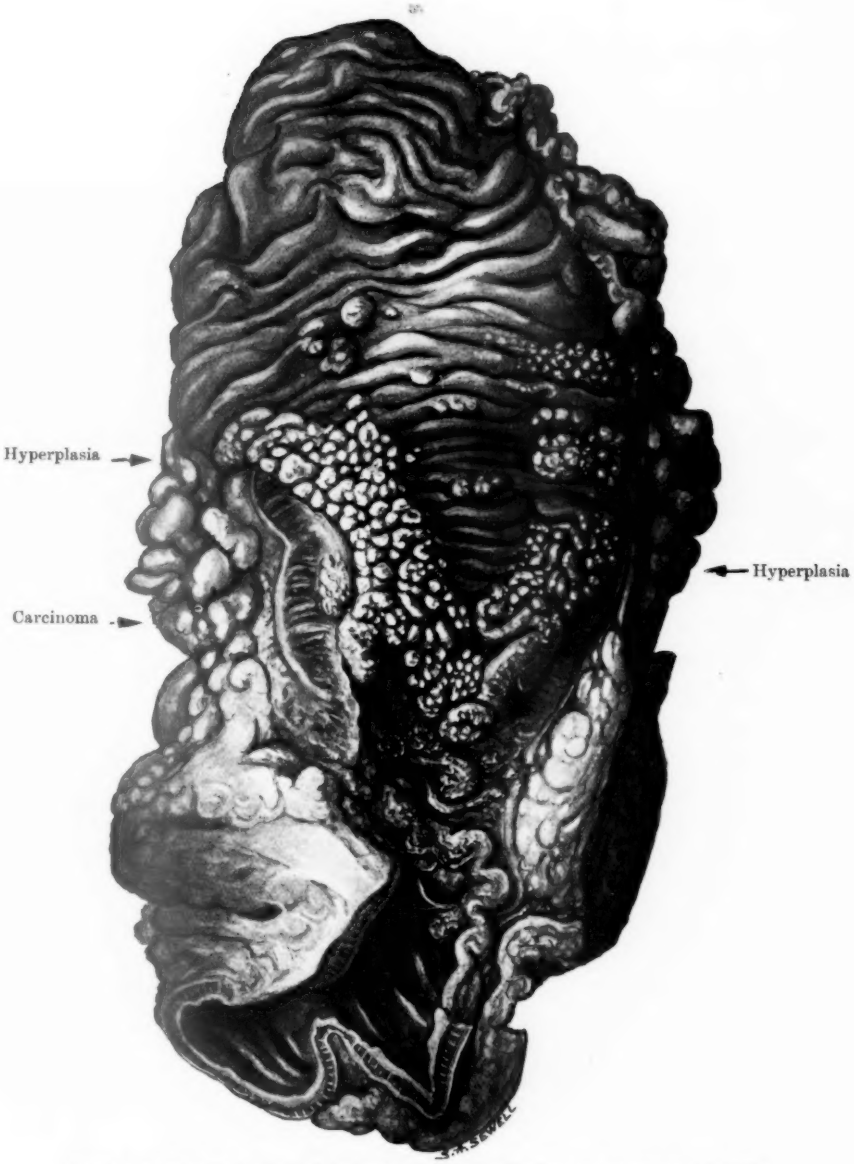

FIG. 4.—Carcinoma of cæcum showing hyperplasia of mucous membraneand multiple adenomata. (Royal Free Hospital Museum.)

FIG. 5.—Carcinoma of rectum with multiple adenomata. (Author's case.)

FIG. 6.—Polyposis intestini with carcinoma of rectum. (St. Mark's Hospital Museum)

FIG. 7.—Constricting carcinoma of descending colon showing pedunculated adenoma above growth. (Author's case.)

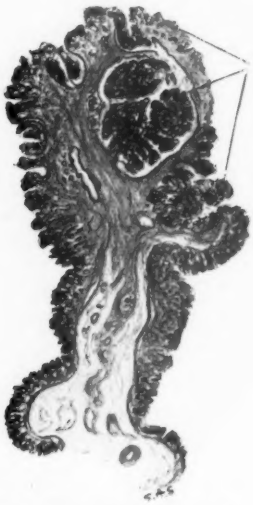

FIG 8.—Pedunculated adenoma removed from pelvic colon showing early malignant changes. (Author's case.)

FIG. 9.—Multiple adenomata of jejunum. (Royal Free Hospital Museum.

Section of Tropical Diseases and Parasitology.

President—J. GORDON THOMSON, M.B.

[*November* 6, 1930.]

Cultivation of the Spirochætes Associated with Tropical Ulcer.

By E. C. SMITH, M.D.

(From the Medical Research Institute, Lagos, Nigeria).

ABSTRACT.—Spirochætes from cases of tropical ulcer have been cultured in a modified Wenyon media and have now been successfully passed through thirty-two subcultures. —A pure culture has not yet been obtained.—Five inoculation experiments are described in which it has been shown that the spirochætes and fusiform bacilli, in mixed culture, are capable of proliferation and of producing ulcerated lesions in natives.

NUMEROUS attempts have been made to cultivate the spirochætes, *Treponema schaudinni* (Prowazek), which are associated with the condition known as tropical ulcer. Mühlens [1] probably was the first to obtain a mixed culture of spirochætes and fusiform bacilli with material taken from a case of tropical ulcer. After three subcultures the spirochætes died out. Sanarelli [2] was successful in cultivating spirochætes from material derived from guinea-pigs. He regards these as being identical with the organisms found in tropical ulcer. Fox [3] working in India on Naga sore was able to cultivate spirochætes in one instance anaerobically. Tunnicliff [4] and Pilot and Brams [5] have described cultures of spirochætes obtained from mouth-lesions, which are of a similar nature to those present in ulcus tropicum.

In Lagos material was obtained from typical cases of ulcer, and attempts were made to cultivate the organism in semi-solid serum, ascitic and hydrocele agar, but were entirely unsuccessful.

Later, a slightly modified Wenyon media was used with positive results. The composition and preparation of the media is as follows:—

Normal saline 320 c.c., 2% nutrient agar, 40 grm. These are mixed in a 500 c.c. flask and autoclaved at 120° C. for ten minutes. After cooling to approximately 37° C., 15 c.c. of fresh human blood are added to it. The contents of the flask, after agitation, are distributed by sterile syphon into culture tubes. At first, long narrow tubes were used and were almost completely filled with the media. This was found to be unnecessary and ordinary test-tubes, half filled with the media, are now used. Before use the culture tubes are incubated for forty-eight hours, at 37° C., to ensure sterility.

Usually the media forms a delicate coagulum in each tube. This seems eminently suitable to the requirements of the organism, for when, as sometimes happens, the blood retracts into a firm clot, leaving a clear layer of serum above, growth is not so readily obtained.

The inoculum is obtained in the following manner. A typical case of tropical ulcer is obtained and the lesion cleared of all gross superficial contamination by means of swabs soaked in sterile water. By gentle application of a tourniquet to the limb, above the ulcer, a clear serous fluid is made to exude therefrom and is collected by means of a sterile pipette. From 0·5 to 1·0 c.c. of this fluid is introduced into the upper half of the column of media in each tube inoculated. The tubes are incubated aerobically at 37° C. and the contents are examined by the dark-ground after three days for the presence of living spirochætes. The inoculum before use is also examined by the dark-ground method to establish the presence of numerous actively motile spirochætes. By making subcultures *en route*, and maintaining them at a suitable temperature, two strains were brought to England and have now been passed through thirty-two subinoculations, made at intervals varying from four to ten days. From a continued examination of these cultures the following facts have been elicited:—

(1) The spirochætes are aerobic. (2) The optimum temperature for growth appears to be 37° C., but a strain was maintained in Lagos at room temperature (27°-30° C.) for a period of one month. Growth was not noted in cultures kept at 0° C. (3) Subcultures are best made every fifth or sixth day. (4) Growth was obtained with difficulty in serum-agar stabs (agar 2 parts, serum 1 part) and after three or four subcultures the spirochætes died out. (5) The organism can be cultivated in a media in which the human blood is replaced by rabbit's blood, but the results are not so certain. (6) The longevity of the organism in the media described and at 37° C. varies greatly. Most of the cultures examined showed no active forms after twelve days. In some, however, living forms were seen after eighteen days' incubation and in one instance after twenty-seven days.

It has not been found possible as yet to obtain pure cultures of the spirochæte. The fact that the organism is aerobic and that its growth in solid media is very uncertain renders the problem of isolation a difficult one. It is hoped that by the application of Barber's single-cell technique to the material obtained from the lesions, as described, a pure culture will eventually be obtained. It is possible, of course, that this spirochæte requires the presence of other organisms for its growth.

Inoculation Experiments.—Although it was not possible to obtain the spirochætes in pure culture it was thought advisable to carry out some preliminary

TABLE OF INOCULATION EXPERIMENTS.

	Subject	Inoculation and site.	Result of inoculation	Microscopical examination
A.	Male, native, aged 28. Convalescent from a chronic ulcerative condition of leg, probably yaws. General condition good	Inoculated intracutaneously with a ½ c.c. of a mixed culture of spirochætes (ninth passage) in left arm. Right arm inoculated in a similar way with "control"	Boil-like reaction on the 5th day. Small ulcer formed by the 7th day. Ulceration active for two days, when healing commenced. Control side negative	Spirochætes and fusiform bacilli present from the 5th to the 7th days. (Dark-ground examination)
B.	Male, native, aged 33. A case of tropical ulcer admitted for scraping. General condition good	Received a ½ c.c. of a spirochæte culture (seventh passage) in left arm. Right arm inoculated with "control"	Indurated area on the 2nd day with vesicle formation. Well-marked bleb-formation on 3rd day. Shallow circular ulcer on 5th day, ⅛" in diameter. Healing began 9th day. Control side negative	Spirochætes and fusiform bacilli present from third day onwards. Spirochætes much more numerous on 7th day.
C.	Native boy, aged 16. Suffering from tropical ulcer of leg. General condition fair	Inoculated in left arm with ½ c.c. of a spirochæte culture (ninth passage). "Control" inoculation on right side	Painful nodule on 2nd day. Purulent bleb on 3rd day. Small ulcer on 4th day. Active to the 7th day when it presented a sharply marked circular lesion ¾" in diameter. Healing began on 9th day. Control side negative	Spirochætes and fusiform bacilli present from 3rd day. Spirochætes much more numerous on the 5th day and until healing commenced.
D.	Male, native, aged 25. Convalescent from a large tropical ulcer of leg. Good general condition	Right arm inoculated with ½ c.c. of an anaerobic culture (sixth passage). "Control" made on left side	Purulent bleb ⅛" in diameter on 2nd day. Shallow well-marked ulcer ¾" in diameter on 3rd day. Increased to 1" by 4th day, covered with purulent slough. Separation of slough complete by 7th day exposing an ulcer 1½" in diameter. Healing 9th day. Control negative	Fusiform bacilli numerous from 2nd day until healing. No spirochætes seen.
E.	Male, native, aged 30. Suffering from guinea-worm. Good general condition	Inoculated in right arm with a ½ c.c. of an anaerobic culture (fifth passage) "Control" made on left side	Indurated painful area on 2nd day. Boil-like lesion on 3rd day. Small ulcer formed by the 5th day, remaining active until the 7th day when healing began. Control side showed a small vesicle on 3rd day, area indurated and purulent on 5th day. Resolution on 7th day without any ulcer formation	Fusiform bacilli present from the 3rd day. No spirochætes seen. Gram-negative intra-cellular organisms seen in smears from control. Pure culture of a pseudomonas obtained on agar.

inoculation experiments. The contaminating organisms were fusiform bacilli and members of the pseudomonas group and since the spirochætes were aerobic it was possible to obtain cultures under anaerobic conditions, which were rich in fusiform bacilli but devoid of spirochætes. Conversely the aerobic cultures showed numerous spirochætes with scanty fusiform organisms. *B. pseudomonas* was common to both cultures and could readily be obtained in pure culture. With the assistance of Dr. B. G. T. Elmes, inoculation experiments were accordingly made, using: (1) aerobic mixed cultures of spirochætes and *B. pseudomonas* (*see* Table—experiments A, B, C); (2) anaerobic mixed cultures of fusiform organisms and pseudomonas (*see* Table—experiments D, E). Further, in the case of all the experiments made, the opposite arm was injected with a "control" which consisted of a strain of *Bacillus pseudomonas* grown in pure culture in the modified Wenyon media.

This control served to exclude possible results due to protein shock or to the action of *B. pseudomonas* alone. No general reaction was noted in any of the five patients inoculated, the reaction being entirely localized to the experimental site. The control side remained negative throughout with the exception of case E, in which a mild boil-like lesion occurred without any ulceration.

Ulcers were produced in the five inoculations made, being particularly well marked in C and D. These ulcers resembled, clinically and microscopically, the type known as tropical ulcer. The natives concerned, being hospital patients, were well fed during the time involved in the experiments and the areas were kept covered with dry dressings or hot fomentations during the active period. Were it not for these applications the lesions might have pursued a more aggravated and prolonged course. The inoculum used was always examined by the dark-ground prior to inoculation.

As volunteers were difficult to obtain, the number of inoculations made was necessarily limited but it is interesting to note that two of the subjects were suffering from tropical ulcer at the time of the investigation and one was convalescent from the same condition. This suggests that the condition affords no immunity to those affected.

Since pure cultures were not available for the experiments described it is impossible to draw any definite conclusions therefrom. They show, however, (1) that the spirochætes in mixed culture are capable of active proliferation when inoculated into the skin of a suitable subject and can produce a lesion resembling that known as tropical ulcer; (2) that the fusiform bacilli in a mixed culture, free of spirochætes, can also proliferate under similar conditions and can produce similar lesions; (3) that *B. pseudomonas*, in pure culture, has little or no pathogenic power when used as described.

It remains to be shown whether the spirochætes, if capable of being grown in pure culture, can give rise to lesions in man. Smith [6] working with fuso-spirochætal diseases of the lungs, has shown that neither the spirochæte nor the fusiform bacillus alone can produce infections in mice or guinea-pigs, whereas positive results are obtained when the above organisms are mixed with a vibrio and an anaerobic streptococcus.

It has yet to be proved that the spirochætes and fusiforms are stages of the same organism or that they are distinct from one another. A study of the literature will reveal the variance of opinion on this important point. Sanarelli [2], Tunnicliff [4], and Rukawischnikoff [7], support the view that they represent stages in the life-cycle of one organism. Pratt [8], Klarenbeek [9], and Gins [10], among others, take the opposite view. In this connection it may be noted that no mutation was observed in experiments D and E. In these two instances fusiform bacilli were present without any spirochætes, up to the seventh day when healing commenced.

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Discussion.—Professor J. G. THOMSON (President) said that recently Neitz and Canham (1930) had studied a similar disease in pigs. In treatment it was found that the intravenous injection of arsenicals such as neosalvarsan had little or no curative action, but if the preparation were injected locally, or applied as a dressing, the results were frequently very satisfactory and in some cases produced a complete cure.

Dr. BROUGHTON-ALCOCK said he congratulated Dr. Smith—who had read this paper at his (the speaker's) request—on some new observations on ulcus tropicum. The successful culture of *S. vincenti* was the first and should help to elucidate the ætiology of this phagedænic lesion. He (the speaker) was fortunate in having seen a late culture of the spiral form in which the characteristic polymorphism of the spirochæte was manifest. He believed that the cyclic stages of the spirochæte included the so-called *B. fusiformis*, and the successful reproduction of the lesion in volunteers with either spiral or fusobacillary forms seemed to support this view. The finding of the latter only in the lesions produced after its inoculation was difficult to interpret, except on the grounds that the fusobacillary forms tended to predominate at the surface and the spiral forms to penetrate the deep tissue. Possibly it was the surface exudate that was examined. [Dr. Broughton-Alcock referred to the successful re-implantation results of Onorato and others, and discussed the questions of insufficient and inadequate diet, which he considered to be an important contributory factor.]

The common sites of the lesions in man seemed to vary with the class of employment, in the endemic areas, and the abrasions thereby incurred.

Sir ALDO CASTELLANI said that he found sulfarsenol, given by intramuscular or intravenous injection useful at times, and asked if Dr. Smith had carried out any investigation as to the means by which the infection was carried: was it by contact, or through some insect carriers, or other animal carriers? Prowazek believed that the spirochæte was carried by leeches.

Dr. HUGH STANNUS said he believed that spirochæte-fusiform infections occurred naturally only after some injury, and that vitamin deficiency and calcium-phosphorus imbalance were important predisposing factors.

Excellent results had been obtained in the treatment of varicose ulcers by the use of electroplast bandages. Had an antigen for diagnostic cuti-reaction been prepared? and did spirochætes reappear when anaerobically grown *B. fusiformis* was subsequently cultured aerobically?

Dr. N. HAMILTON FAIRLEY considered that Dr. Smith's experiments supported the view that tropical ulcer was of infective origin and directly transmissible through local inoculation. He asked if Dr. Smith had filtered his cultures and subsequently tested the infectivity of the filtrate.

Dr. ANDREW ROBERTSON said he would like to ask Dr. Smith whether, in his opinion, there was a diminution in the virulence of *Treponema schaudinni* as a result of cultivation over a prolonged period, and, secondly, if Dr. Smith considered that *T. schaudinni* possessed a degree of host specificity. He asked these questions in view of his experiments (carried out with Dr. Smith's strain of spirochætes in culture) on rabbits. Intradermal inoculations of the cultured treponemata into rabbits, on the back, the groin and the scrotum, had all proved to be negative despite the fact that, in some instances, local damage to the tissues had been previously produced by injection of a minute quantity of a dilute solution of potassium

hydroxide. Small necrotic lesions, which healed rapidly, formed at the sites of injection of the alkaline solution, but in none of these could spirochætes be discovered, nor did typical "tropical ulcer" result.

Further, attempts to continue the cultivation of the treponemata isolated by Dr. Smith on medium of the same composition as that used in the original experiments, but using rabbits' instead of human blood, had also been unsuccessful. It seemed possible—in view of Dr. Smith's ready success in producing lesions in man by injections of culture, and also of the virulence exhibited by the parasite, which, if not identical with *T. schaudinni*, was certainly very closely allied—in the leg lesions and ulcers of pigs, that certain animals were much more susceptible than others. The difficulties of producing experimental ulcers had been noted by other workers, e.g., Strong and Shattuck, in Brazil, who found that ulceration could be produced by the experimental inoculation of *T. schaudinni* into dogs, only after the tissues were damaged or bruised in some way.

Dr. J. NEIL LEITCH referred to some investigations recently made in Kenya under the Rowett Research Institute. The incidence of tropical ulcer was not correlated with that of malaria or syphilis, but might be modified by parasitic infestation. It appeared to be closely associated with malnutrition, and seldom occurred in meat- and milk-fed tribes.

The occurrence of ulcer was associated with low blood-pressure, low hæmoglobin index, and abnormal levels of blood-calcium and phosphorus. Both calcium and phosphorus were higher than in normal natives, the phosphorus markedly so. Since the level of blood-calcium in normal natives was lower than that in Europeans, and since the higher blood-calcium in ulcer cases was not associated with any improvement in condition over normal cases, it was probably associated with the high blood-phosphate. Analysis of the diet of these natives showed it to have a deficiency of calcium (and a marked relative surplus of phosphorus) as compared with the level shown to be necessary for calcium equilibrium.

In Sierra Leone he had assisted Dr. R. A. Elliott in Schick-testing a large number of natives. Only one Schick-positive reactor was found in twenty ulcer cases tested, whereas similar types without ulceration showed a much larger number of Schick-positive. A Klebs-Loeffler infection had been found in other tropical ulcers, e.g., Barcoe rot and veld sore. Both the diphtheria bacillus and Vincent's organism which occurred in throat infections in temperate climates were skin infectors in tropical climates. He believed the most important factor in causation to be defective diet. In addition to mineral sufficiency, fat-soluble vitamins were most effective in producing a cure.

Dr. E. C. SMITH (in reply) said that the President's remarks with reference to the disease in pigs suggested the use of these animals for experimental purposes.

He (Mr. Smith) had no experience of treatment by sulfarsenol as mentioned by Sir Aldo Castellani. With regard to the method of infection, that always seemed to be a direct one, through an abrasion or minor injury.

In reply to Dr. Stannus, he thought that for economic reasons the electroplast treatment was not advisable in West Africa. No antigen had been prepared in Lagos, but as some of the successful inoculations had been performed in natives who had suffered from tropical ulcer, it would seem that there was no immunity present. Spirochætes were not found to reappear in anaerobic cultures of *B. fusiformis* grown anaerobically.

He was grateful to Dr. Fairley for his suggestion of testing the activity of filtered cultures and he proposed to try this as soon as an opportunity offered.

Dr. Robertson's query as to whether there was a diminution of virulence resulting from cultivation could probably be answered positively, though of course there had been no means of making inoculations in humans whilst in England. Host specificity undoubtedly existed, as experiments made in animals in Lagos (rabbits, white rats, guinea-pigs, monkeys) were in the main unsuccessful.

Dr. Leitch's remarks were more or less borne out by the work of Dr. McCulloch in Nigeria. He (Dr. Smith) thought it advisable not to regard dietetic deficiency as a complete explanation of tropical ulcer, until the organism involved had been demonstrated to be non-pathogenic. Pure cultures were, of course, essential.

[*April* 3, 1930.]

Generalized Infection of Muscles with *Cysticercus cellulosæ*; measurements of cysts and comparison with those of *Trichinella spiralis*.

By W. Broughton-Alcock, M.B., and M. Weinbren, L.R.C.P., M.R.C.S., D.M.R.E.

Dr. Broughton-Alcock: The patient, a man now aged 47, gave as past history that he left England as a regular soldier to serve in the South African War, after which he served in India and Burma from 1902 to 1912.

In 1912 he was invalided from the Service because of three fits, epileptiform in character, while in camp on return from India. Such fits did not return, and until wounded in France during the late war he was in good health.

He states that he never has felt ill, or suffered from muscular spasms or rheumatic pain. He is not aware of ever having had a tapeworm or of being associated with anyone so infected at any time before the onset of the fits.

On physical examination no abnormality can be felt in any skeletal infected muscles, and the patient can freely use them. In fact, were the calcified cysts not seen at the time of taking a radiological picture to determine a lesion of the knee due to a gunshot wound, they would probably not have been found or the patient have been conscious of them.

Dr. M. Weinbren: The patient was sent to the X-ray Department with the tentative diagnosis of "?Sequestrum following gunshot wound of thigh."

The film showed a number of opaque bodies in the soft tissues. The remainder of the body was consequently radiographed. The opaque bodies were present in the muscles of all the limbs, the abdomen, chest and face (masseter muscle). None was detected in the brain. They were oval shaped, were lying parallel to the muscle fibres (see fig. 1) and were obviously some calcified parasite.

I reported a similar case with Dr. Graham Hodgson in 1926,[1] and we then suggested that the parasite in question was *Trichinella spiralis* because of its shape and distribution. The only difficulty about such a diagnosis was the size of cysts seen, and it was assumed that a great deal of calcium had been deposited not only in the cyst but around it.

On measuring the cysts in the present case by means of a grid placed in the same plane as one of the limbs at the time of the exposure, the parasite appeared to be approximately $\frac{1}{4}$ in. long, while that of the *Trichinella* is only 400μ in length.

I did not consider that excision of one of the cysts for microscopical examination was justified in this case. It was obvious the cysts were not doing any harm. The patient was in a septic condition and even a small incision would very probably have become infected.

Of course, I accept Dr. Leiper's opinion that the cysts were those of *Cysticercus cellulosæ* and not those of *Trichinella*.

[1] M. Weinbren and A. K. Graham Hodgson, *Lancet*, 1926 (ii), 174.

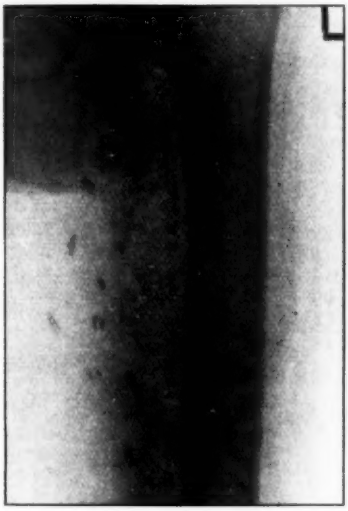

FIG. 1.—*Cysticercus cellulosæ*.

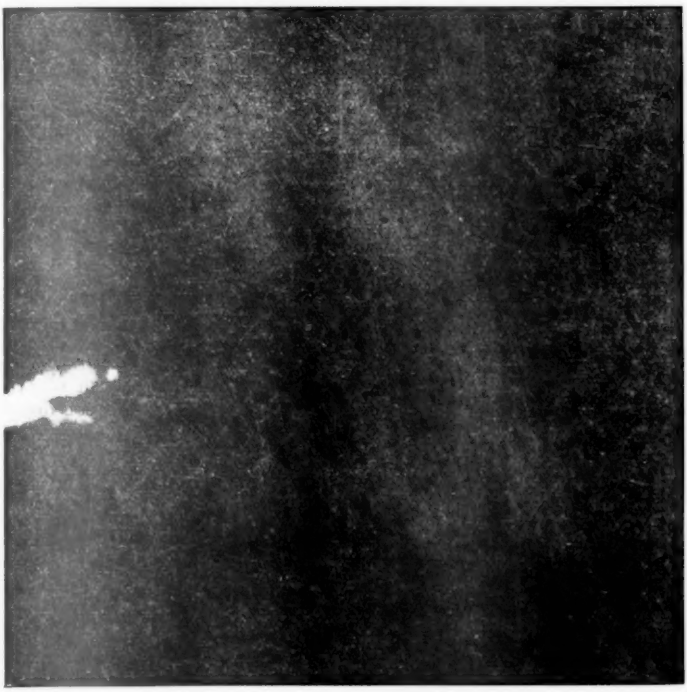

FIG. 2.—*Trichinella spiralis* in muscle. (× 4 dimensions.)
From the Museum of the Royal College of Surgeons.

POSTSCRIPT.—Since the last meeting, Dr. Leiper kindly arranged with Sir Arthur Keith for me to radiograph some of the specimens of trichinosis from the collection of the Royal College of Surgeons.

Two specimens, one a piece of the biceps and the other a portion of the trapezius, were examined. Both had come from the dissecting rooms of the Middlesex Hospital in 1865.

The cysts show up in the films as minute specks and can be seen in the prints with the naked eye, but they are too small to be reproduced on a slide, or for publication. Enlargements of about 4D were consequently made (fig. 2).

[The authors wish to express their thanks to Sir Lisle Webb, Director General, Medical Services, Ministry of Pensions, for allowing them to publish this case, to Dr. Leiper for his help, and to Sir Arthur Keith for permission to radiograph the specimens.]

Section of the History of Medicine.

President—Sir HUMPHRY ROLLESTON, Bart., K.C.B., M.D.

The Secrets of Alexis. A Sixteenth Century Collection of Medical and Technical Receipts.[1]

By Professor JOHN FERGUSON, M.A., LL.D., F.S.A.

[This paper was read by Dr. A. P. Cawadias at a meeting of the Section held on May 7, 1930. It was among the manuscripts unpublished at the time of the death of the author who was Regius Professor of Chemistry at the University of Glasgow from 1874 until 1915. Professor Ferguson's MSS. and a large section of his valuable Library are now in the possession of the University of Glasgow.]

ABOUT the middle of the sixteenth century there was published a handbook of practical receipts, which, to judge from the number of editions in Italian, and of the versions in other languages, must have achieved extraordinary popularity. The book has a permanent value as a record and must be reckoned with in every history and bibliography of technology. No treatise better illustrates the popular or household practice of applied chemistry, of the arts, and of medicine, at its date, than that which passes under the name of Alexis, or Alessio, of Piedmont.

Considering the variety and extent of its contents, its literary interest as displayed in successive editions, and the obscurity which shrouds the personality of the author and the origin of the book, one might have expected that some attempt would have been made to elucidate both the secrets and their compiler, himself the greatest secret of all. Since nothing of the kind exists my endeavour shall be to supply it.[2]

PART I.—THE AUTHOR.

The edition of Alexis' treatise, printed at Venice in 1557, in 4°, which is the earliest I have seen, contains an address to the reader by Alexis, in which he describes the events which led to the compilation of his secrets. As this address emanates, apparently, from the author, and is a characteristic composition, it will be as well to give it entire and allow him to tell his story in his own way. I quote it in the words of the English translation of 1558.

1 Read to the Society of Antiquaries, London, February 11, 1897.

2 In the references to Alexis which I have made elsewhere, I have confined my attention to problems connected with the first and early issues of the work, and have not discussed the biography of the author. The "Bibliographical Notes on Histories of Inventions and Books of Secrets," were published in the *Transactions of the Archæological Society of Glasgow*. They may be briefly enumerated here. In Part I (*Trans.*, *II*, pp. 189-190) there is bare mention of the editions of Venice, 1568, London, 1595; inaccurate besides as to one or two other dates. In Part II (*ibid.*, *II*, p. 251), Bas. 1560, 1563, German 1573; p. 258, Lyons 1558; p. 262, index. In Part III, pp. 218-224, there is a discussion as to the date of the first edition, and translations are enumerated in Italian, French, English and German. In Part V (*ibid.*, pp. 446-450) there is a discussion on the language of the first edition and a notice of Wecker's translation into Latin. In the first supplement (*Trans. Arch. Soc.*, p. 24, paragraph 22) there is a notice of several rare or undescribed editions in Italian, Latin, French and Dutch, besides some in English.

" They that have knowen me in time past, or to speake plaine, haue vsed me familierly all my lyfe time, can peradventure, tel how God by his great goodnes, hath made me to be borne of a noble house and bloude (according to the commune, I will not saye vayne, perswasion of them, that stablish nobilitie more in the merites of another man, than in our own) and that besides this I have alwaies had my pleasures and great plentie of richesse, yea farre passing the smalnes of my desertes, I will say yet more (not to boast or to anaunce my self, but to the ende to refourme the gentill reader, and to geve thankes vnto God) that there be many whiche knowe, how I being given even from my first youth vnto study, have gotten, not onely the knowledge of the Latin, Greke, Ebrue, Caldei, and Arabic tonge, and also of divers other nations and countries. But aboue al thinge havinge by a natural inclination, taken a singuler pleasure in Philosophy, and in the secretes of nature, have wandered and travailed abroad in the worlde the space of xxvii[1] yeares, to the intent to acquainte my self with all sortes of learned and discrete men. By the which diligence and curiositie, I have learned many goodlye secretes, not alonely of men of great knowledge and profound learning, and noblemen, but also of poore wenie artificers, peysantes, and all sortes of men. Moreover I have ben thre times in Levant, and sondry times have travailed almost all other partes of the world, without resting or seiourning at any time in one place aboue v moneths. Now this my study and desire of knowledge, as well of the vniuersall sciences, as of particuler secretes, and althoughe it was geven vnto me by nature, as to the most part of men (for every man by an instinete of nature desyreth to knowe thinges) yet have I alwayes been noseled vp by a certain ambition and vainglorie, to knowe that, whiche an other should bee ignorannte of: whiche thynge hath grafted in me, a continuall niggardnesse or sparing, to distribute or communicate any of my secretes, yea vnto my moste singuler frendes that I had: saying, that if the secretes were knowen of every man, thei should no more bee called secretes, but publike and common.

Now, it chaunced these fewe daies past, being in Milan: in the fowerskore and twoo yere, and seven monethes of myne age, that a poore artificer was moruelously tourmented with the stone, and had been twoo daies without making his vrine. The Cyrurgen that dressed him hym, knowying well that I had many secretes, and singulerly for the stone, came to me, and requested me that I would teache hym the receipte, or at the least to give hym the medecine, composed and ready made, for the health of the patiente. But I perceiuyng that he would vse other mennes thinges, for his owne profite and honour, refused to give it hym, but willed hym to bryng me vnto the sicke man, and that I my self would minister the medecine vnto him *gratis*. The Phisition, either fearying blame if it should be knowen, that he had recourse to the aide of an other man, havyng peraduenture, bosted that he had the secrete hymself, or els in the mean tyme, still to make his profite in dissembling the matter, and differryng it yet twoo daies more, with duiers excuses and colours, vntill he brought me to the patiente, whom at my commyng I founde so nigh his ende, that after he had a little lifted up his iyes, castyng them pitiously towards me, he passed from this into a better life: not havyng any neede, neither of my secrete nor any other receipt to recouer his health. With this cace I was moued to soohe a compassion and sorowe, that not onely I wished my self evill, but also I desired to die: seyng my ambition and vain glorie, to have been the cause that this poore man was not succoured with the remedy, and gifte that God the father, and Lorde of vs all had given me. Wherefore, so greate was the remorse of conscience in me, that, desiryng to sequestrate my self fro the worlde, and not findyng my self of soche a disposition of mynde that I could live in a Monasterie among religious menne, better edified then I, I was at the laste fully resolved with my self, to choose a place separate from any Toune, where I have a little lande, some bookes, and a studie, for to avoide idlenes. Here I live a life, whiche I call a Monkes life, with one servaunte, whiche goeth to the toune, not to begge, but to buie my prouision, and other thynges necessarie: for to sustanie his poore life and myne, as long as it shall please God.

But yet not havyng the power to put out of my fantasie, but that I was a verie homicide and murtherer, for refusing to give the Phisition the receipt and remedie, for the healyng of this poore man, I have determined to publishe and communicate to the world, all that I have, beyng assured that fewe other menne have so many as I. And mindyng to set forth none, but soche as bee most true and proued, I have these daies paste (taken partly out of my Bookes, and partly out of my memorie, all those that came to hand) made a collection of soche as I am certaine bee veritable, true, and experimented, not caryng if some of theim

[1 This is a mistake of the English translator. In every edition in Italian and other language it is " fifty-seven," which corresponds better with the narrative.]

be written, or printed in any other Bookes then this. For of this my collection the reader, as touchyng those, maie at the least take this vtilitee and profite, that whereas before he mought have doubted, whether soche remedies sette foorthe by an other manne, were true or not, he shall bee now assured, vnder the affirmaunce of my faithe: For truely, I should not sette my self (beeyng in the age, and disposition, bothe of bodie and mynde, that I am nowe in) to write fables or lies, that should continue alwaies. But of one poyncte I wille aduertise the reader, and that is, that he dooe the thynges with good diligence, and that in medecines concernynge mannes body. he vse the ayde and helpe of phisitions: Although in dede many of theim, moued with a certaine rustick, and euyll grounded enuie, with a passion of Jalousy, are want to blame and contempne thinges that come not of them selves. Wherefore. as wel in this, as in euerye other pointe, if he that will vse these, should perchaunce finde, that the thing would not take effecte according to his contentation, lette him beware that he abuse not him self in the confection of them, and to beginne againe with more diligence. Assuringe him selfe, that (as I have sayd) there is nothing in this boke but is true and experimented. And geving alwayes glory and praise vnto god onely for all, have a good hope, that, by meane of his divine grace, I will consequently make you a present of the rest of all that I have gotten in so manye

trauayles, voyages.
costes, and
diligente studye.

Farewell.

In this statement two dates are involved, the author's age, and the year of writing. The author was 82 years and 7 months old when the adventure which he relates befell him, When did he first publish this narrative? Postponing criticism of this question to the bibliography, let it be assumed that the book took six months to prepare and print, and let it also be assumed that it did not appear before 1555. Alexis would be by that time in his 84th year and must therefore have been born about 1471. In the book there is confirmation both of the date and of Alexis' statements. The allusions may be taken in chronological order.

The following is the earliest date I have noticed. Alexis would be 33 or 34 years old, by the above calculation. Speaking of the plague he furnishes a number of receipts against it. Of one of them—a rather "scunnersome" mixture—he says: "Et fu prouato nella inclita Citta di Venezia 1504, per Mattio calegaro che staua a Santa Sofia, & prouollo sopra à se & sua mogliere." "It was tried in the renowned city of Venice in 1504, by Matteo Calegaro who dwelt at Santa Sofia and proved it on himself and his wife."[1]

Among the preparations of most worth is the "oil of a red-haired dog," the constituents and preparation of which are detailed with great minuteness. The dog was to be seethed whole in the oil till it fell to pieces and with it were then to be mingled scorpions, worms, various plants, hog's and ass's marrow and a number of other things in a definite order, and the ointment or oil thus got was endowed with important virtues. Three cures by it are mentioned. A man of Alexis' acquaintance found much ease from it in an attack of gout.

"And the said griefe returning againe foure times at sondrie times, yet anoynting himselfe therewith three times (as is aforesayde) the paine came vnto hym no moore in the space of three yeares that wee were in Rome together, which was the year 1514. And thys man was called *Diego*, a Portugall, and dwelte at the mount Jordan. Sith that Tyme, being gone to Venise and from thence into Leuaunt, I have heard nothynge of him."[2]

The Italian original, however, gives a glimpse of the author and his friend which the translator has unkindly left out—Diego was a notary and Alexis did not know

1 Ex Ed. Pesaro, 1557, f. 45 *vreso*. In the English translation (1558, f. 38. *recto*) all about Mattio Calegaro is omitted and only the place and date are given.

2 *The Secretes of Alexis*. English, 1558, f. 18 verso. The Italian is much more elegant (Pesaro, 1557, f. 22 *verso*): "et quel mio amico si chiamaua Diego Portughese, che era sollecit atore, & habitaua a Monte Giordano. Dapoi io mi parti da Roma, & audai a Venetia, & poi in Leuante, & non ho mai piu inteso muoua di lui se sia uiuo o morto, che benedetto sia sempre doue si troua, perche ueramente era persona molte uirtuosa, & di bonissima uita."

whether he was alive or dead "but may he be happy wherever he is, for he was indeed a most worthy man and of irreproachable life." Alexis therefore went back to Venice from Rome, probably to get a ship going to the East.

There seems to be no doubt as to his having gone to the Levant from Venice, for he had, while there, another opportunity of testing the curative power of this same ointments. He says:

"As I came from Jerusalem in the yeare 1518 in a shippe, of the whiche the maister was called Peter de *Chioggia*, we were set vpon by fiue foystes of Pirates, on this side *Corphu*, and one of the mariners so attainted with the stroke of a gonne that he had his arme brused and broken, and with the same blowe and another hurt in the brest."[1]

Where he was going to on this voyage does not appear, but the next we hear of him is that he was in Syria in 1521,[2] and there learned that the "great Lordes of the Moores" used a piece of red hot gold laid on the place to prevent the growth of hair on their children. He seems therefore to have stopped in the East for some years, travelling about, for he was at Aleppo in 1523, and there saw a man, a Milanese, who had the plague, and who had boils on his thigh and arm, cured by the use of a powder of ivy berries.[3]

Nothing more is vouchsafed by Alexis as to his whereabouts for twenty years, and then we find that he had returned to Italy. The notice, though brief, is a most important one. It relates to a decoction of plants, which is excellent for a "stitch in the side, or pleuritike Apostumes."[4] "This water," he says, "was given me at *Bolonia*, the yeare 1543, of a gentilman, called Girolamo Russelli, with the which, the same yeare, he was healed of the same disease."

Once more, there is an account of a third wonderful cure by the "oil of a red dog" already mentioned. A monk of the order of S. Onuphrio, had his left arm sapless so that it looked exactly like the stump of a branch of a tree. Alexis had it rubbed with the oil in the sun until it dried in and after fifty-six days treatment the arm began to show signs of improvement. Nine days later the arm was as full of flesh as the other. This was in the summer of 1547, but no place is mentioned.[5]

The year following, 1548, Alexis was back again at Venice and there saw the effects of a certain water in healing wounds. The servant of a noble man, called Leonello Pio de Carpe, received a dagger wound on the instep, and it was rapidly healed by the application of a little of this water.[6] There are other references in the book to foreign countries which presumably Alexis visited, but as they are vague and are unaccompanied by dates, they are of no value as biographical data.

Finally about the year 1553 or 1554 he was in Milan and met with the adventure which he says led to writing his book and in 1555, according to Brunet, it was published. The year after, he was in Venice, and undertook the revision of the first part of his book. The bearing of this will be considered more particularly in the second section of this paper. It is also said that he died in 1565—but so far as I know, there is no authority for that date.

1 Pesaro, 1557, f. 21, *verso*, English 1558, f. 18, *recto*.

2 Pesaro, 1557, f. 92, *recto*. English 1558, f. 80 *recto*.

3 Pesaro, 1557, f. 49, *verso*. English 1558, f. 42, *recto*.

4 Pesaro, 1557, f. 27, *verso*. English 1558, f. 22, *verso*.
"Questa acqua mi fu data in Bologna, l'anno 1543 da lSignor Girolamo Ruscelli . . ."

5 Pesaro, 1557, f. 21, *verso* English, 1558, f. 18, *recto*. This version differs in some points from the original. The original is as follows:—". . . io ne ho vista es perienza in un frate di santo Onuphrio . . . che haveva il braccio sinistro tutto secco, che parea vevamente un tronco di ramo d'arboro; . . . & io lo feci ungere con questo sopradetto unguento ooglio al sole, che era di state, l'anno 1547, & cosi lo facea ungere . . . & las ci arlo al sole, che fosse tutto ascuitto & penetrato nel braccio. Et in cinquantasei giorni si cominciò a veder manifestamente che le vene tornavano a dar nutrimento al membro. Et in noue altri giorni sequenti il braccio fu rierupito di carne come l'altro . . ." The English version runs thus: ". . . I caused him then to be annointed with this saide oyle (which I had set in the sonne the somer of the year 1547) . . . and made him tarie in the sonne untill the saied oyle was cleane dryed up, and had perced thorowe the saied arme: and within lv. daies (sic) men did perceyve . . . that the veynes gave nourishment . . ."

6 Pesaro, 1557, f. 17, *verso*. English, 1558, f. 15, *recto*.

There can be no question that all this hangs perfectly well together. If one looks very closely into the few facts that are available, one may detect a flaw here and there which rather adds to their genuineness and spontaneity. Thus Alexis in his address says he never stayed more than five months in a place during his travels, and yet he speaks of residing three years in Rome. I would attach little importance to such a discrepancy, for after all Alexis may not have intended his "five months" to be taken strictly, or to apply except to foreign countries. It seems to me also, that he leaves too little time for the composition of his book. That, however, rather confirms the view that he was working in an offhand and natural way without other design than to acquaint the reader with how it came to pass that he wrote the book at all. Even that objection he has partly anticipated by saying that the book was composed in a great hurry and sent with all its defects to be printed.

The most important item of the whole, in the light of what I shall bring forward presently, is the statement under date 1543, that he got from *Girolamo* Ruscelli, in Bologna, a draught good for "pleuriticke aposthumes."

Such then is the biographical sketch which we gather from Alexis himself, and it has been accepted without question by most of the subsequent writers I have consulted. When, moreover, a subsequent preface by Alexis referring to the publication of the book is considered—a preface about the accuracy of which there can hardly be a doubt—it is difficult to refuse credence to the address of Alexis.

And yet I personally cannot help feeling that there is a false note in it; that while the facts are not discordant, the words of the preface and the spirit of it are so, distinctly. In the account of his studies, journeys and acquisition of knowledge from the humblest sources, there is such a curious resemblance to what Paracelsus tells about himself that one may be struck at least by the coincidence even if one grant that it may be fortuitous, and that Alexis independently followed the same methods, and did not simply copy Paracelsus' statement. But my hesitation to accept the story arises rather from the tone of the address to the reader as a whole. There is in it a self-glorification and a self-abasement which tally only in so far as one extreme is apt to beget its opposite. He feels the responsibility of the patient's death, but the remorse is enhaloed with a certain pride, that he, if any man, had the secret that would have effected the required cure. The consequent and immediate change from secrecy to publicity; from travelling for a life-time all over the world to settling down in a lonely lodging; from mixing with all classes of people on those journeys to shutting himself up like a hermit; from vaunting good birth and multifarious learning to recognizing his worthlessness that kept him from joining a holy fraternity; from abundance of riches to the impoverishment of an anchorite, with one servant who bought the provision for their "poor life", is bewildering in its almost pantomimic rapidity, and it has engendered in me much doubt as to whether it be true or whether it must be regarded as a specimen of a medical advertisement of the sixteenth century.

In the year 1567 there was published at Venice a collection of receipts ascribed to Jeronimo Ruscelli, which it seemed might clear up all obscurity connected with Alexis. This book is mentioned by a few authorities, but the accounts are very vague. The book is excessively rare but there is a copy in the Bibliothèque Mazarine at Paris. It contains however only the first part, though that is what appears to be of most importance for the identification of Alexis. There is a completer copy containing both parts, in the Biblioteca Nazionale at Florence. The book may be described as follows:—

Secreti Nvovi | Di Maravigliosa | Virtv | *Del Signor Jeronimo* | *Ruscelli* | *I quali continouando a quelli di Donno Alessio,* | *cognome finto del detto Rvscelli,* | *contengono cose di rara esperienza,* | *& di gran giouamento.* | *Con Privilegio.* | . [Device] | In Venetia, | Appresso gli heredi Marchiò Sessa. | MDLXVII. |

Small 8vo. Signatures : a, b, c, *A* to *Z*, in eights : or ff. [24] 184. Printed in italics. The device is Pegasus in the clouds soaring over a landscape with mountains. The title is surrounded by a border of scrolls, faces, and figures.

Collation :

a 1 Title.

a 2 *recto*, Sansovino's letter, which ends a *z recto*.

a 3 *verso*, Tavola di Tutti li Secreti, which ends e 8 *r* : Il Fine della Tavola | di i secreti del Signor Ieronimo Ruscelli. | The verso is blank.

A 1 *r*. The Proemio begins, and ends *A* y *v* (ff. 1-7).

A 8 *r*. The text begins, and ends *Z* 8 *v* (ff. 8-184).

At the end of the text : Il fine della Prima Parte.

In the Mazarine Copy the words " Prima Parte " have been partially erased.

In the copy at Florence the first part agrees with the preceding. The second part runs on continuously with the first in signatures and folio numbers, without a title page.

Aa ∧ *r* Heading of scroll work and Masks. | De Secreti Del | Sig. Jeronimo Rvscelli | Da Viteibo, | Parte Seconda. | — | A far bianco sofistico.

8vo. Signatures *Aa* to *Nn* in eights ; or, ff. 185-287. 288 probably blank, is wanting. Printed in italics like the first part.

At the end, *Nn* 7 *r* (f. 287 *r*.) : *Il Fine Della Seconda* | *Parte De' Secreti.*

Nn 7 *r*, *Registro.* * *A B C D E F G H I K L M N O P Q R S T V X Y Z*, *Aa Bb Cc Dd Ee Ff Gg Hh Ii Kk Ll Mm Nn.*

Tutti sono Quaderni. | In Venetia, | Apresso li heredi di M. Marchiò Sessa. | M DLXVII. |

This copy wants *Nn*1.

It may be observed that the " Tavola " at the beginning contains the titles of the receipts in both parts.

A notable thing is that while the preliminary matter occupies three sheets, marked a, b, c, the Registro takes no notice of them but gives one sheet marked * only. The explanation of this discrepancy which suggests itself to me is that originally there was only enough preliminary matter to fill a sheet, but after the work had been printed off it was found necessary to enlarge it, but by that time of course the Registro could not be altered. It is a bare possibility that a copy of the *Secreti Nuovi* of Ruscelli exists somewhere which contains one sheet marked *, instead of the three marked a, b, c.

The foundation for Sansovino's statement is, I suppose, what is affirmed by Ruscelli in the *Proemio*. That has next to be considered.

It contains a lengthy account of the origin and organization of an Academy, or Society, for scientific experimental research. He narrates that when he was living in the Kingdom of Naples—some years before he went to Venice—in a " famous town," the name of which he does not specify, and being in a company of twenty-four persons of distinction along with the Lord of the district, this Philosophical Society was founded. He gives details of the original twenty-four members, who with three additional members made up the mystic number of twenty-seven : their social position, nationality, income, and the contributions which they respectively paid into the Society's exchequer. Altogether the Society was able to lay out usually five thousand gold crowns (scudi) per annum. He next describes the various people employed by this " Academia " ; two apothecaries or druggists, two goldsmiths, two perfumers, a painter, four herbalists, all of whom were kept at the Society's expense, with suitable salaries. There were, besides, two classes of servants, those who attended to the affairs of the house, and to everything connected with the daily life of the inmates, and those who were employed solely in the work of the " Filosofia " —as it was called—as in carrying water, pounding, building furnaces, looking after

the fires, vessels, lutes and all other duties connected with the experimental operations, and these were the assistants of the specialists above mentioned.

On the first Sunday of every month there was a meeting of the whole staff, when reports were given in of all that had been doing since the previous meeting.

The primary design was to study and investigate natural phenomena in order to become better acquainted with them. To this was added the employment of the knowledge thus acquired in Medicine and the arts required for human wants. The members wished to instruct themselves and to benefit the world at large by bringing to certainty and true knowledge so many most useful and important secrets of all kinds, for all sorts and conditions of people, rich and poor, learned and unlearned, male and female, old and young. They thus continued for some years to make constant experiments upon secrets, whether mentioned in printed books or in old or new manuscript collections.

Next follows an account of the house, or laboratory "which we call by its own proper name La Filosofia." It is unnecessary here to go into the details of the selection of the site, the plan and style of the building, and the working appliances which it contained. It is extremely interesting as showing that in Italy, nearly three hundred and fifty years ago, there had been thought out a scheme for a Society which, in a suitable house, should carry out systematically researches particularly into the chemical properties of matter, and into the applications of the results to Medicine and technology. The scheme is one more proof, that in Italy in the sixteenth century classical literature and antiquities were not the sole subjects of study, or the only paths to culture. When Ruscelli has concluded the description of the building, its courts and recreation grounds, he proceeds:

> In this place (the courtyard) we often met and discussed what we did daily, and here I collected all the secrets following and those earlier ones which I published a few years ago of Donno Alessio Piemontese, the which in truth were all collected in the aforesaid Academy and were tried and found out by our successful company.

And he concludes this *Proemo*, or introduction, by saying that, according to their rules, he published his collection with the permission of the "Principe" and the associates, and makes reference to the severe illness which had reduced his strength and confined him constantly to his bed. From this illness he died before he could print his new collection, and so it came into Sansovino's hands. Unfortunately neither Sansovino's dedication, nor Ruscelli's Proemio, is dated. Thus there is no indication in it of the year of Ruscelli's death.

The ascription of the work to Ruscelli, possibly on the strength of the preceding, was apparently first made by his contemporary Jeronimo Muzio in a passage quoted below. The same view was held in 1583 by Ciaconius,[1] who, after quoting the book and its translations, says: "Hieronymus Ruscellius is the author, and he published it under the pseudonym of Alexius Pedemontanus." He gives no authority for this remark, though it is obviously based on the *Secreti Nuovi*.

Considering what Sansovino says in his dedication about Ruscelli's fame, one might conclude that something was known about him. But this is the first difficulty that presents itself: who was Hieronymo Ruscelli of Viterbo, the alchemist? I have not met with his name in any of the histories of that subject. The chief person of the name with whom I am acquainted was the author of *Letters*, but after inspecting many catalogues I have met with nothing like the present work under his name, and nothing to identify the two Ruscellis.

It will not have been forgotten that, in his desire to give every one due credit, he tells his readers that a receipt for the cure of "pleuriticke apostumes" was imparted to him at Bologna in 1543 by a gentleman called Girolamo Ruscelli.

[1] *Bibliotheca Libros et Scriptores ferme (auctos ab Initio Mundi ad annum MDLXXXIII ordine Alphabetico complectens.* [Ed. J. E Kapp.] Amstelodami et Lipsiæ, 1744, col. 94.

Certain comments can be made on this statement, though it is hard to say which one, if any, can be justified. Firstly, it may be that we have here a bit of by-play on the part of the author to preserve his incognito. Hieronymo Ruscelli, the author, calling himself Alessio or Alexis, drags in his own name as the authority for a certain preparation. It has been done rather cleverly, because he has quoted this name only once. Several allusions to it would have been clumsy, and might have raised suspicion, but by a dexterous single reference precisely the desired effect has been produced and the reader is thrown off the scent of the authorship. No one would suspect that the pseudonymous author, Alexis, would quote himself as an authority under his own name, Ruscelli, as a personal acquaintance. If, however, the statements by Sansovino, Ruscelli and Muzio be accepted as true, one must be also prepared to believe that Ruscelli did treat himself as a friend of Alexis—in other words, such an interpretation of Alessio's one reference to Ruscelli is required (could be put forward only because it would be required) to justify the statement that Alessio is identical with a pseudonym for Ruscelli. The whole thing is unsupported by any evidence, and I doubt whether those who have insisted upon the identification on the strength of Sansovino's preface are aware of this allusion to Ruscelli in the text of Alexis.

If, instead, it be assumed that Alessio's narrative is as reliable as Sansovino's, this reference supplies a distinct proof that Alessio is quite a different person from Ruscelli, with whom, however, he was acquainted and in communication. In this view, which is simple and straightforward, and is therefore more likely to be the true one, Alessio gives his authority without any ulterior design whatever.

There is a possible third interpretation, namely that Hieronymo Ruscelli, the alleged author of the book, is a different person from Hieronymo Ruscelli the authority for the secret in question. There is, however, absolutely no evidence on the point and one could be driven to entertain it at all only as another way of supporting the truth of Sansovino's allegation without sacrificing one's belief in the honesty of Ruscelli. The only thing that can be said in its favour is that it is preferable to the first explanation—being honest.

As in the case of Alexis' story, so in this of Sansovino and Ruscelli, any attempt to controvert or criticize it is useless. There are no facts against it, and the claim is advanced with such an air of uncontradictable certainty, that one must accept or reject it as a whole, for every other story is not only excluded, but is not even noticed.

It may be admitted that Ruscelli's Academy is quite as plausible as Alexis' patient. There is something besides very fascinating in the conception of such a society, and apart altogether from the truth or falsity of the narration, and apart from whether or not the idea was ever embodied and carried out, it is a most striking proposal to have been started in the year 1567.[1] But did it exist?

With regard then to the two versions of the origin of this collection of practical receipts, my conclusion, notwithstanding my doubts as to the genuineness of Alexis' remorse, is this: neither may be true, or either may be true, but it is impossible that both can be true. If either be true I am inclined to favour the older story. First, just because it was first in the field, before there was any inducement to alter it; secondly, because it is supported by internal evidence in the first part, both by dates and by the mention of Hieronymo Ruscelli as a distinct personage. Third, because the only reason to doubt it is a willingness to assent to the account of the origin of the collection. Fourth, because Ruscelli's claims rest on a series of fictions.

Sansovino's account, based on Ruscelli's, on the other hand, came out ten or twelve years later, and while he professedly gives the true statement of the authorship, he never once takes notice of Alexis' preface. Sansovino must have known what

[1] The account of the Academy would seem to point to the *Academia Secretorum Naturæ*, founded at Naples in 1560 under the presidency of Baptista Porta. This however existed for only a brief period. Tiraboschi, *Storia della Letteratura Italiana*, VIII, 153.

Alexis said about his parentage, travels and mode of collecting his information, and yet he repeats an absolutely incompatible view of the matter without ever hinting that they are so. Ruscelli says that Alexis' Secrets were collected in this Academy. This is not only quite different from what Alexis says, but it ignores his account altogether; passes it by as if it had never existed. Now was Ruscelli the author of Alexis' preface, and if so what was his object in prefacing the book with a deliberate fabrication—not to use a terser word? If he was not the author of it how does it come there at all, and being there why does he not notice and repudiate it as a tissue of untruths? But if he was the author of it, what proof is there that his elaborate description of an experimental Academy which existed for at least ten years is not equally untrue? We should have only his word to go by in both cases. And yet twelve years later he ignores it and gives another account which is quite incompatible with it and the later account of the origin of the Secrets.

Whatever opinion may be formed after a critical examination of the preceding statements regarding the authorship of the *Secreti* of Alexis, and the *Secreti Nuovi* of Ruscelli, there is no doubt about the existence af both Ruscelli and Sansovino. A brief recapitulation of what is said about them is almost necessary in connection with the present question. (The book, with Alexis' preface, went broadcast for centuries—that with Ruscelli's claim never reached a second edition—and I know of only the two copies described above.)

Jeronomo or Girolamo Ruscelli was a native of Viterbo. From his earliest years he was trained in the best learning and while still a lad was received into the Court of Cardinal Marini Grimani, and followed him to Aquileia, or rather Utini. From there, he was sent at the expense of the Cardinal, who admired his talents and ability, to Padua where he completed his studies as a diligent pupil of Donatus of Verona and Buonamici of Bassana. He accompanied his patron to Rome and began to shine amongst those most distinguished for their learning, and as it was the fashion of the time to cultivate elegance in speaking and writing, he turned all his attention to this object, and endeavoured to illustrate his native tongue in numerous writings. He soon became famous throughout Europe for his erudition, but, like Ludovico Dolce, his school companion and the dearest of his friends, he remained poor.

He died at Venice at a comparatively early age, and was buried in the same grave with Dolce. There is some confusion about the date of his death. The year 1569 is stated, but this cannot be correct if the *Secreti Nuovi* which appeared in 1567 was published after his death according to Sansovino. In that case the year 1565, as given by Dela Monnoye, is more likely to be correct.

He was the author of numerous works, lists of which are given by several writers. They consist of annotations on Boccaccio, Ariosto, Giovio, &c., &c.; extracts from the poets, letters of princes, commentaries on the Italian language, rules of Italian verse, and similar literary and critical topics. By none of the authorities is there any allusion to the *Secreti Nuori*, to Ruscelli as the author or to Sansovino as the editor of it.

Whether Muzio gave the true reason or not, the secrecy or pseudonymity which Ruscelli wished to maintain seems to have been well preserved: "per avventura fece egli questa metamorfosi in virtù della sua alchimia, donde ne nacque il libro publicato sotto il nome di D. Alessio di Piemonte."[1] Muzio, if anyone, ought to have known the facts, for he was not only a contemporary of Ruscelli, but corresponded with him, and one letter at least is extant.

The parts of this book (besides the title-page) which are of importance for my present purpose are the dedication by Sansovino, the editor, "Al Magnifico et Eccellente M. Antonio Maria Poiana Gentilhuomo Vicentiuo." and the introduction,

1 *Lettere del Mutio Iustinopolitano*, Vinegia, Gabriel Giolito, 1551, 8°, f. 127.

or "Proemio," by the author Signor Ieronimo Ruscelli, which occupies the first seven leaves of the book. I shall state briefly what these contain relative to the identification of Ruscelli and Alexis.

In his dedication Sansovino speaks as follows :—

> Ieronimo Ruscelli, a man of great learning, who took much pleasure in Alchemy, was well known in our days for his many gifts. Having, in the years gone by, learned from the art many valuable secrets respecting medicine, as well as about minerals and metals, and wishing to confer some benefit on the world, he gave to the press under the feigned name of Donno Alessio of Piedmont, the first part of his labours, with such good success, that from then till now, everybody knowing the profit to be derived from those secrets, they have been printed and are still printing in an infinite number. Whereupon Ruscelli stirred by this, to the end that he might furnish the best conclusion to his ventursome beginning, put his hand to the second part, in which he has striven to supply what was perchance lacking in the first; and having brought it to a due close, and being forestalled by death, left it to his heirs and relations[1] to publish. This second part, which forms the present work, has come to my hands from the said heirs, and as it is not meet that it should be hidden away, so as to defraud the needy in their occasions of the good to be obtained therefrom, I have at last put it out under your illustrious name; and not without cause: for, being a man naturally disposed to assist others, you making open profession of the same: it has seemed to me, that the perusal of it, which abounds with profit, would be agreeable to you. . . .

In this (as in the title-page) there is no uncertainty. Ruscelli published his first collection under the pseudonym of Alexis, and this after gatherings in this second part were put out under his own name, subsequent to his death, perhaps from the illness which he himself mentions in his Proemio.

I do not put forward what has now been said as by any means the last word on the subject, because it is possible that there are unused, because unknown, sources of information, which may settle the matter definitely in favour of one of the alternatives which I have shown to exist, or in some other way which I have not anticipated. Possibly among the *Secreti nuovi* there may be some allusion which would solve the difficulty, but I have not had the opportunity of reading that book through. I have meantime done no more than state the difficulties and contradictions; I am far from saying that Ruscelli was not the real Alexis, still farther that he could not be; but it would require a great deal more than a claim advanced by him or an affirmation made by him, self-convicted as he stands of contradictory stories, to make me believe that he was.

Part II.—Bibliography.

If a book has a wide circulation over a long period, it of necessity supplies a want, and the teaching must influence to a great extent the ideas of its readers and those who put its directions in operation. In this sense therefore the work of Alexis may be regarded as one of the most important productions of the sixteenth century. Reference to the printed table will show that the book was published in parts at successive dates.

The first part consists of six books, and this must be regarded as the genuine work of Alexis, whoever he was. This part is practically the same in all the editions and translations which I have consulted. It is different, however, with the second, third, and fourth parts, which are quite different in some of the editions and versions.

Confining our attention in the meantime to the first part, the editions of it which I have seen, viz., the 1557 French and 1558 English, agree in containing only a preface, and Alexis' address to the reader. But in the earliest edition of the Italian, whether of Pesaro or Milan (2), there is another preface of Alexis in which he gives an account of his version of the work.

[1] The Italian word is "nipoti," nephews or grandchildren, but as there is no evidence as to Ruscelli having been married, I have preferred the indefinite word.

In the epistle prefixed to the Italian of 1557 he tells us that in the previous year, actuated by the motives consequent upon the death of the man whom he had refused to assist until it was too late, he had compiled the first part of his Secrets.

The first draft, which he distinctly states was in Latin, was sent on in such a hurry to Venice to be printed that he had no opportunity to make a fair copy, and so it went ill written, muddled, and full of additions and corrections.

A few months later he heard that it had appeared in Italian, and was welcomed by everybody, for all which he was most grateful and returned thanks to God. He was busy at the time with a second part containing secrets of great importance, when having occasion to visit Milan he saw a copy of the book and bought it. On examination he found it very well done on the whole; but whether from the defective penmanship or errors in it or imperfect corrections, he observed a number of faults and inaccuracies in the copy he had bought. For this reason and hearing that the book was out of print, and that it was going to be reprinted, he postponed the publication of the second part and revised, corrected and enlarged the translation of the first part.

From this it would appear that the book was first written in Latin, translated from the MS. into Italian and published in Venice. This second preface was prefixed to an edition of 1557—and the "previous" year 1556 was that in which the book seems to have been first compiled and printed—which, however, does not tally with Brunet's edition of 1555.

If the author's statement is to be taken literally, viz., that the first edition appeared in 1556, then either Brunet or the author is misinforming us. It is possible, however, that the preface in which he tells us this was really written in 1556 a little before the book was printed, and then the *previous* year would be 1555—and Alexis would be referring to Bordogna's edition, which appeared in 1555. All this, however, is pure hypothesis—an attempt made to reconcile Alexis' preface with Brunet's date.

If one could only see a copy of the first edition what an amount of discussion and talk would be saved!

One thing is quite certain: Alexis' original Latin was never printed.[1] What came of it? It is rather absurd when we remember that in 1559 the first part was translated into Latin by Wecker and in his preface he says he translated it to keep up his knowledge of Italian, which he had acquired by residence in the country, and secondly to make a good book more generally accessible.

Looking about him for one suitable for his purpose, he encountered Alexis' work, which he at once set about translating from Italian into Latin. In his preface Wecker makes no allusion to an original Latin edition. It is most unlikely that Wecker, who was living in Italy when the book first came out, would not have known whether it was in Italian and had been in Latin first.

He certainly goes clearly on the assumption that there was no Latin version before his own and says so distinctly on the title-page. So that after all, and in spite of the elaborate mendacity—shall I call it, of Ruscelli we have not got Alexis' original work at all. His Latin was rendered into Italian by a person—name unknown—and the Latin we have was made from the Italian and not by Alexis!

The French edition is distinctly made up and contains a quantity of matter which does not occur in the Italian at all and is certainly not by Alexis. The English translation was made from the French, not from the original Italian. This is obvious from a comparison of the three apart altogether from the statement of the translator.

In particular what is called the third part contains a translation of a series of tracts which appeared originally in German and in Dutch in the first half of the

[1] "Bibliographical Notes on Histories of Inventions and Books of Secrets," Glasgow Archæological Society's *Proceedings*, 1885.

sixteenth century, passed through a variety of forms and were in part translated into English.[1]

I have given elsewhere[2] an account of all the editions of these tracts and their varieties, amounting in all to about fifty and stretching from 1531 to 1720. This tract is also contained in the English translation. The present paper therefore supplies a completed view of what I know at present about one of the most important of all the books of secrets—which I have attained only after some familiarity with the class of literature to which it belongs.

The following list is arranged according to languages with a separate short chronological table.

When the name of the Library is not given, the description is drawn from a copy in the author's own possession.

[1] 1557. B.M. 42. f. 19. De' Secreti del Reverendo Donno Alessio Piemontese, Prima parte, diuisa in sei libri. Opera vtilissima, et universalmente necessaria, & dilettenole à ciascheduno. Ora in qvesta seconda editione dall' autor medesimo tutta ricoretta, & migliorata. Et aggivutovi nel fine d'ogni libro molti bellissimi secreti nuoui. Con privilegio dell illustrissima Signoria di Venetia, & altri Principi, per anni XV. | In Venetia per Comin da Trivco. M.D.LVII. | Small 4°.

This is the author's genuine second edition. The second letter is in none of the other copies and the additions to the 2nd, 4th, 5th and 6th books are wanting also. These will be found in the French edition of 1557.

[2] 1557. SECRETI DEL | REVERENDO DONNO | Alessio Piemontese, Nuouamente posti in luce. | Opera vtile, Et Neces. | saria vniuersahnente a ciaseuno. | [Device] | M DLVII. | In Pesaro per Bartholmeo Cesano. Small 8°.

[3] 1557. Univ. Lib. Bologna. A. IV. F. VIII. 57. Imperfect copy of the first part of Alexis in six books in 4° ($8\frac{2}{16} \times 5\frac{8}{16}$) This seems to be the first edition in the British Museum.

[4] 1557. B.M. 7460. aa. Les | SECRETS | DE REVEREND | SIGNEVR ALEXIS | PIEMONTOIS. | Contenans excellens remedes contre plusieurs maladies, playes, & autres accidens, Auec la maniere de faire distillations, parfuns, confitures, teintures, couleurs, & fusions: Oeuure bien approuué, tres vtile & necessaire a vn chacun. | Traduit d'Italien en François | [Device] | EN ANVERS, | De l'Imprimerie de Christofle Plantin | 1557. | Avec PRIVILEGE. | Small 4°.

[5] 1557. Lübeck Stadtbibliothek. Les | Secrets | De Reverend | Signevr Alexis | Piemontois. | Contenans excellens remedes contre plusieurs maladies, playes, & au- | tres accidens, Auec la maniere de faire distillations, parfuns, con- | fitures, teintures, couleurs, & fusions: Oeuure bien approuué, tres- | vtile & necessaire a vu chacun. | Traduit d'Italien en François. | [Device of the Compasses with the motto: Labore et Constantia.] | En Anvers, | De l'Imprimerie de Christofle Plantin. | 1557. | Avec Privilege. | Small 4to.

[6] 1557. Les | Secrets | De Reverend | Seignevr Alexis | Piemontois. | Contenans excellens remedes contre plusieurs maladies, playes, & au- | tres accidens,

1 Refers to the "Kunstbüchlin" or "Kunst Boeck." In the *Proceedings of the Philosophical Society of Glasgow*, 1888-1894. "Some Early Treatises on Technological Chemistry," supplement, 1894.

2 *Proceedings of the Phil. Soc. Glasgow.* The original MSS of full bibliography with collations and signatures is to be consulted in the Glasgow University Library.

Auec la maniere de faire distillations, parfuns, con- | fitures, teintures, couleurs, & fusions: Oeuure bien approuué, tres- | vtile & necessaire a vn chacun.—Traduit d'Italien en François. | [Device]. | En Anvers, | De l'Imprimerie de Christofle Plantin. | 1557. | Avec Privilege. | Small 4to.

This contains the first part in six books. It is the first edition in French.

[7] 1557. B.M. 1038, i, 34. SECRETI DI DON | ALESSIO PIEMONTESE NVO | VAMENTE STAMPATI. | Con vna Bellissima Aggivnta De | Secreti hauti da un religioso pratickissimo, | exellente, & esperimentati. | Vbi consulueris mature opus est facto. | Per Vincenti Busdrago MDLVII. | Small 8°.

[8] 1558. (G.U.L. Bdl.—1.25). DE' SECRETI | DEL REVERENDO | DONNO ALES— | SIO PIEMON— | TESE, | Prima parte, diuisa in sei libri. | OPERA VTILISSIMA, | & vniuersalmente necessaria, & di— | lettenole à | ciascheduno. | ORA IN QVESTA SECON | da editionè dall' autor medesimo Urtla ricorretta, & migliorata. | ET AGGIVNTOVI NEL | fine de ogni libro molti bellissimi secreti nuoui. | In Lyone, | Per Theobaldo Pagano, | 1558. | Small 16°.

[9] 1558. St. Genevieve. LES SECRETS | DE REVEREND SEI— | GNEVR ALEXIS | PIEMONTOIS. | Contenans excellens remedes, contre plusieurs ma— | ladies, playes, autres accidens, Auec la ma— | niere de faire distillations, parfums, confitures, teintures, couleurs, & fusions. Oeuure bien ap— | prouué, tres-utile & necessaire à vn chascun. | [mendcroll device]. | A PARIS, | 1558. | 16°.

According to Brunet this is one of the rarest and most prized of all the editions.

[10] 1558. B.M. 1038, d, 35 (3). LA SECONDA | PARTE DE I SECRETI | DI DIVERSI ECCELLENTISSIMI huomini nuouamente raccolti, & con | diligenza stampati. | CON PRIVILEGGIO DEL | ECCELLENTISSIMO SENATO | DI MILANO PER | ANNI DIECI. | IN MILANO | M. D. LVIII. | 8vo.

[11] 1558. B.M. 1038, d. 35 (3). La Seconda Parte De I Secreti Di Diversi Eccle— | lentissimi *huomini nuouamente raccolti, & con* | *diligenza stampati*. Con Privileggio Del Eccellentissimo | Senato Di Milano Per Anni Dieci. | In Milano *Appresso di Giouann' Antonio de gli* | *Antonii*. M. D. LVIII. *Al segno del Leone*. Sm. 8vo.

[12] 1558. De' Secreti | Del Reverendo | Donno Ales- | sio Piemon- | tese, Prima parte, diuisa in sei libri. | Opera Vtilissima, | & vniuersalmente necessaria, & di- | lettenole à ciascheduno. | Ora In Questa secon | da editione dall' autor medesimo tutta ricor- | retta, & migliorata. | Et Aggiontovi Nel | fine de ogni libro molti bellissimi secreti nuoui. | [Device] | In Lyone, | Per Theobaldo Pagano, | 1558. | Small 16°.

[13] 1558. The | Secretes | Of The Reverende | Maister Alexis Of | Piemornt. | Containyng excellente remedies against | diuers diseases, woundes, and other accidents, | with the manner to make distillations, | parfumes, confitures, diynges, co- | lours, fusions and meltynges. | A worke well approued, ve- | rye profytable and ne- | cessary for euery man. | Translated out of Frenche into English, | by Wyllyam Warde. | Imprynted at London by Iohn Kingstone | for Nicolas Inglande, dwellinge in | Poules churchyarde. | Anno. 1558. | Mens. Nouemb. | Small 4°.

Black letter, except the contents of each paragraph and the running title in italics. The Index is in black letter.

[14] 1559. B. M. 1036. c. 1. (1—3). DE' SECRETI DEL | REVERENDO DONNO | ALESSIO PIEMONTESE | PRIMA PARTE DIVISA | IN SEI LIBRI. | [Device]. | IN MELANO. | Appresso di Giouann' Antonio de gli Antonij. | M D LIX. | 8vo.

[15] 1559. DEI SECRETI | DI DIVERSI ECCELLEN- | TISSIMI HVOMINI | NVOVAMENTE RACCOLTI | & con diligenza stampati | parte terza. | [Griffon] | IN MILANO | Appresso di Giouan' Antonio de gli Antonij. | M D LIX. | 8°.

[16] 1559. B.M. C.31 d. 12. The | Secretes | Of The Reverende | Mayster Alexis Of | Piemornt. | Conteinyng many excellēt Remedies agaynst | dyuers diseases, woundes, and other accidentes, | with the manner to make Distillations, | Parfumes, Confitures, dyinges, co- | lours, fusions, and Meltynges. | A worke wel approued, ve- | rye profytable and ne- | cessary for eue- | ry man. | Translated out of Frenche into Englishe, | by Wyllyam Warde. | Londini. | Anno à virgines partu. | M. D. LIX. | Small 4°.

Black letter. The running title, and headings of the section are in roman.

[17] 1559. LA SECONDA PARTE | DE I SECRETI DI DIVERSI | Eccellentiss. huomini nuouamente raccolti, | & con diligenza stampati: | CON PRIVILEGIO DEL ECCEL | lentissimo Senato di Milano per anni dieci. | [Device of the Griffon] | IN MILANO | Appresso a Giouann' Antonio de gli Antonij. | MDLIX. | 8°.

[18] 1559. Bibl. Roy. B, 27. ix. 94.—SECRETS, OV | RECEPTES SOVVRAINES, | Bien Experimentées et Ap- | provvees par Divers | Avtevrs. | CONTENANTES SINGVLIERS | Remedes contre diuers maladies: | Auec plusieurs autres sciences artificielles, fort | profitables à vn chacun. | [Device of compasses.] | A ANVERS, | De l'Imprimerie de Christophle Plantin, | 1559. | AVEC PRIVILEGE. |

This part contains the Kunstboeck receipts.

[19] 1559. LES | SECRETS DV | S. ALEXIS PIE- | MONTOIS, | DIVISEZ EN SIX LIVRES: | Ausquels auons adjoint | AVTRES SECRETS DE NOVVEAV | adjoutez par iceluy, qu'aucuns ont appellé, | le Second Volume: | & | LES RECEPTES DE DIVERS AVTEVRS | toutes biens experimentées, & approuuées. | Lisez l'Auertissement: Page 3. | [Device of Compasses.] | A ANVERS, | De l'Imprimerie de Christophle Plantin | 1559 | AVEC PRIVILEGE. |

[20] 1559. ADIOINCTES | FAITES AVS SECRETS | DE | DON ALEXIS PIEMONTOIS: | MISES EN LVMIERE PARTIE | par le mesme Auteur, & en partie recueillies du la- | beur de plusieurs, qui d'iceus en ont | fait les experiences. | Le tout nouuellement traduict de l'Italien. | [Device of Compasses.] | A ANVERS, | De l'Imprimerie de Christophle Plantin: | 1559. | AVEC PRIVILEGE. |

[21] 1559. Bibl. St. Genevieve.—D. ALEXII | PEDEMONTANI | DE SECRETIS LIBRI | SEX MIRA QVADAM RE- | RUM VARIETATE REFERTI | ex Italico in latinum ser- | moné nunc primum | translati. | PER IOANNEN IACO- | lium weckerum, medicum | BASILEÆ | Anno M. D. LIX. | 8°.

[22] 1559. La Prima Parte | De' Secreti Del | Reverendo Donno | Alessio Piemontese, | Nvovamente Dall' Avttor | Medesimo Rivedvti et | Ricorretti. | [Device]. | Con Priuilegio dell Illustriss: & Eccellentis. Signor Duca d'Vrbino, | che niuno possa quest' opera stampare, ne altroue stampata uen— | dere pertutto il Dominio di sua Eccellenza. | In Pesaro Per Bartolomeo Cesano. 1559. | Small 8vo.

La Seconda Parte | De' Secreti Del | Reverendo Donno | Alessio Piemontese, | & d'altri eccellentissimi huomini. | Nvovamente Madati In | Luce A Commune Vtilita | D'Ognivno. | [Device as above] [Privilege as above] In Pesaro Per Bartolomeo Casano. 1559. | Small 8°.

The first part contains Alessio's address to the reader, and the contents, followed by the text. Part two also contains an address, the contents and the text. It is in six books. The second part does not agree with the second part in English.

[23] 1560. D. ALEXII—PEDEMONTANI DE | SECRETIS LIBRI SEX | mira, quadam rerum varietate re— | ferti ex Italico in latinum ser— | monem nunc primum | translati. | PER IOANNEM IACO— | bum weckerum, medicum. | [DEVICE] | ANTVERPIAE, | In oedibus Ioannis Latij. | M. D. LX. | 24°.

[24] 1560. ALEXII PE— | DEMONTANI DE SECRETIS LIBRI MIRA | quadam rerum varietate vtilitateq ; re— | ferti, longe castigatiores & amplio— | res quàm priore editione. | Nam sex prioribus, septimus accessit ex eius— | dem authoris appendice factus : omnes ex Italico | sermone in Latinum conuersi. | Io. Iacobo weckero Basiliensi Medi— | co interprete. | BASILEÆ, | APVD PETRVM PERNAM | M. D. LX. Small 8°.

[25] 1560. Ste. Genevieve.—EMPIRIE, | ET SECRETS | DV S. ALEXIS | Piemontois, | Diuisez en six liures. | PREMIERE | PARTIE. | Auec vne table generale, du | contenu en iceux. | [Device]. | A LYON, | PAR GVIL. ROVILLE. | A L'ESCV DE VENISE. | — | 1560. 16°.

[26] — Empirie, | Et Secretz | Dr S. Alexis | Piemontois, | — | Seconde | Partie. | — | Auec vne table generale, du | contenu en iceux. | [Device] | A Lyon, | Par Guillaume Rouille. | 1561. | Auec priuilege du Roy. |

La | Troisieme | Partie Des Secrets Or Receptes Sou | ueraines, experimentées & | approuuées par diuers | Auteurs. | Continuant les liures du Seigneur | Alexis Piemontoys. | — | Auex vne table generale de toutes les ma- | tieres contenues audit Liure. | [Device] | A Lyon, | Par Thibauld Payen. | 1561. | 16°.

All printed in roman.

The Kunstbüchlein receipts are in part III, pp. 143-240, beginning Pour endurcir le fer.

[27] 1560.

The device looks like a mace or ornamental iron pillar, erect on a stone, with two birds at the foot of the pillar and round it is the legend RES PARVAE CRESCVNT CONCORDIA. and below is the imprint ANTVERPIAE | In œdibus Ioannis Steelisii. | M. D. LX.

[28] 1560. Hunt. As. 2. 27 & Hunt. As. 2. 26 both want leaves. ¶. The seconde | part of the Secretes of Ma- | ster Alexis of Piemont, by hym col- | lected out of diuers excellent | aucthours, and newely transla- | ted out of Frenche into | Englishe, with a | generall Ta- | ble, of all the | matters conteined | in the saied | Boke. | By Willyam Ward. | ¶. Imprinted at London, by Jhon | Kyngston : for Nicholas | Englande. | Anno domini. M.D.lx. | Sm. 4°

[29] 1560. Amiens. D. ALECII | PEDEMONTANI DE | SECRETIS LIBRI SEX | mira quadam rerum varietate re- | ferti ex Italico in latinum ser- | monem nunc : primum | translati. | PER IOANNEM IACO- | bum vveckerum, medicum [Device] Antverpiae, In œdibus Ioannis Steelsij. M. D. LX. | Small 24°.

[30] 1561. Les | Secrets Dv | Seignevr Alexis | Piemontois, | Divisez en Devx Parties | et chacvne D'Icelles | en six Livres. | Les Receptes de Divers | Autueurs toutes bien experimentées, | & approuuées. | [Device] | A ANVERS, | De l'Imprimerie de Christophle Plantin, | au Compas d'or: l'An | M. D. LXI. | Avec Privilege Dv Roy. | 8°.

La seconde Partie | Des Secrets Dv Sign. | Alexis Piemontois | Et D'Avtres Ex- | cellens Av- | ctevrs, | Divisee en Six Livres. | Traduicte nouuellement d'Italien en François. | [Device]. A ANVERS, | De l'Imprimerie de Christophle Plantin. | M. D. LXI. | Avec Privilege dv Roy. |

Secrets, ov | Receptes Sovveraines, | Bien Experimentées Et | Approvvées Par | Divers Av- | tevrs. | Contenantes Singvliers | Remedes contre diuerses maladies: | Auec plusieurs autres sciences artificielles, fort | proffitables à vn chacun. | A Anvers, | De l'Imprimerie de Christophle Plantin, | au Compas d'or. l'An | M. D. LXI. |

The device on all three title pages is a pair of compasses describing a circle, with the motto: Labore et Constantia.

[31] 1561. De Secreten van— | den Eervveerdigen | Heere Alexis | Piemontois. | Inhoudende seer excellente ende wel gheappro— | beerde Remedien, teghen veel—der—hande cranek= | heden, wonden, ende andere accidenten: Met de | maniere van te distilleren, perfumeren, confituren | maken, te verwen, coleuren, ende gieten. | Wt den Françoise ouergeset. | [Device]. | Thantvverpen, | By Christoffel Plantijn, inden gulden Eenhoren. | 1561. | Met Privilegie. | 8vo.

The first edition in Dutch. Contains the first part in six books. Compare the French edition of 1557.

[32] 1562. The secretes of the reverend Maister Alexis of Piemont: Containing ex— | cellent remedies against divers diseases, woundes, and other ac— | cidentes, with the maner to make distillations, parfumes, con— | fitures, dyinges, colours, fusions, and meltings. | A worke well | approued, verye profitable and necessarie for euerye man. | Newely corrected and amended, and also somewhat | enlarged in certaine places, which wanted in ths fyrst edition. Translated oute of Frenche into Englyshe, by William Warde. | [Device] | Prynted at London by Rouland Hall | for Nycolas England, dwellynge in Pater noster rowe. | ——1562. | Small 4°.

The first part is divided formally into six books.

[33] 1562. The thyrde and last parte of the Secretes of the reverende Maister | Alexis of Piemont, by him collected out of di— | vers excellent Authours, with a necessary Table in the ende, conteyning all the matters treated of | in this present worke Englished by | Wyllyam Warde.— [Device.] PRINTED AT LONDON | by Roulande Hall, for Nycholas Englande. | 1562. | Small 8°.

This part is divided formally into six books.

[34] 1563. B.M. Tpe second part of | the Secretes of Maister Alexis of Piemont, by hym col— | lected out of diuers excellent aucthours, | and newly translated out of French into English, | with a generall Table, of all the matters | contayned in the sayde Booke. | By Willyam Ward. | [Device.] Printed At London By Rov— | land Hall, for Nicholas Englande. | 1563. | Small 4°.

[35] 1563. Ham. BC. 11. d. 20. D. Alexii | Pedemontani | De Secretis Libri | Septem, | A Ioan. Iacobo Ve— | ckero Doctore Medico, ex Ita— | lico

sermone in Latinum conuersi, & | multis bonis Secretis aucti. | Accessit hac editione eiusdem weckeri opera, octa | uns de | artificiosis uinis liber. | Basileae. | Apvd Petrum Pernam | M. D. LXIII. | Small 8°.

[35] 1563. DE' SECRETI | DEL REVERENDO | DONNO ALESSIO | PIEMONTESE, | PARTE TERTA. | DI NVOVO RIVE DVTA, COR— | retta, & ampliata in piu luoghi, | CON LA SVA TAVOLA PER | trouar le ricette con ogni commodità. | CON PRIVILEGIO. | [Device as before] | IN VENETIA | Appresso Antonio de gli Antonii. M D LXIII.

[37] 1563. B.M. 7321 aaa. DE' | SECRETI | DEL REVERENDO | DONNO ALESSIO | PIEMONTESE, | PRIMA PARTE. | DI NVOVO RIVEDVTA, COR- | retta, & ampliata in piu luoghi, | CON LA SVA TAVOLA PER | trouar le ricette con ogni commodità. | CON PRIVILEGIO. | IN VENETIA. | Appresso Antonio de gli Antonii. M D LXIII. | 8vo.

In this part all the extra receipts of the Venice 1557 edition are given.

Part II. DE' | SECRETI | DEL REVERENDO | DONNO ALESSIO | PIEMONTESE. | PARTE SECONDA. | DI NVOVO RIVE DVTA, COR- | retta, & ampliata in piu luoghi, | CON LA SVA TAVOLA PER | trouar le ricette con ogni commodità. | CON PRIVILEGIO. | [Same Device.] | IN VENETIA. | 8°.

[38] 1564. St. Genevieve.—LES | SECRETS DV | SEIGNEVR ALEXIS | PIEMONTOIS, | DIVISEZ EN | deux parties, & chascune d'i- | celles en six liures : | AVEC | LA TROISIESME PARTIE | des receptes de diuers autheurs, toutes bien | experimentées & approuués : Con- | tinuant les liures dudict Sei- | gneur Alexis. | AVEC VNE TABLE GENE- | rale de toutes matieres coutenues | audict lieure. | LE TOUT REVEV ET | augmenté oultre les precedentes impressions. | [Device ; Pelican feeding its young. Motto : EN MOY LA MORT : EN MOY LA VIE.] | A Paris. | —— | 1564. | 16°.

[39] 1564. Secretos de Don | Alexo Piamontes, diuididos en | seys libros, llenos de marauillosa diffe- | rencia de cosas : Traduzidos de lengua | Latina en Castellana, por el Li- | cenciado Alonso de | Sancta Cruz. | [Device]. | En Anvers | En casa de la Biuda de Martin | Nucio. Año M. D. LXIIII. | Con Gracia y Preuilegio. | Small 16 mo.

[40] 1564. Empirie, | Et Secrets | Dv S. Alexis | Piemontois. | * | Diuisez ex six liures. | Premiere | Partie. | Avec vne table generale, du con- | tenu en iceux. | [Device] | A Lyon, | Par Gvillavme | Roville. | 1564. | 16 mo.

Empirie, | Et Secretz | Dv S. Alexis | Piemontois, | | Seconde Partee. | | Auec vne table generale, du | contenu en iceux. | A Lyon, | Par Gvillavme Roville. | 1564. | 16 mo.

La | Troisieme | Partie Des Secrets | Ov Receptes Sovverai- | nes, experimentées & approu- | uées par diuers | Auteurs. | * | Continuant les liures du Seigneur | Alexis Piemont- | oys. | — | Auec vne table generale de toutes les | matieres contenues audit Liure. | [Device] | A Lyon, | Par Gvillavme Roville. | 1564. | 16 mo.

[41] 1568. Caius Coll. Camb.—D. Alexii | Pedemontani | De Secretis Li- | bri Septem. | A Ioan. Iacobo | Veckero Doctore Medico, | ex Italico Sermone in Latinum con- | versi, & multis bonis Secretis | aucti, diligentius ca- | stigati. | Accessit eiusdem Vueckeri opera, octa- | uus de artificiosis uinis liber. | Editio Tertia. | Basileæ | Apvd Petrvm Pernam | M. D. LXVIII. | 8°.

Inferior reprint of the 1563 edition.

[42] 1566-68. J. a. St. John's Coll. Cant.—The seconde parte of | the Secrets of Maister Alexis of | Piemont, by him collected out of di- | uers excellent authors, and nevvly tran- | slated out of French into English. | With a generall Table of all the matters | conteyned in the sayde | Booke. | By William Warde. | [Device] | Imprinted at London by Henry | Bynneman, for Iohn Wyght. |

Small 4°. Black letter, except the letter, headline, titles to the sections and Table in roman. The device is the female holding the horses.

[43] 1566.—The thyrde and last | parte of the Secretes of the reue- | rende Maister Alexis of Piemont, by | him collected out of diuers excellent Au- | thors, with a necessary Table in the | ende, contayning all the mat- | ters treated of in this pre- | *sent worke. Englished by* | Wylliam Warde: | [Device] | *Imprinted At Lon* | don by Henry Denham, for | John Wyght. |

Small 4°. Black letter.

[44] 1568.—DE' SECRETI | DEL REVERENDO | DONNO ALESSIO | PIEMONTESE, | PRIMA PARTE. | CON LA SVA TAVOLA PER | trouar le ricette con ogni commodità. | IN VENETIA, | Presso Giorgio de' Canalli. | M D LXVIII. | Sm. square 8°.

It contains physic and dietary rules for each month (January-December) almost identical with those in Raoul du Mont Vert, but fuller and more detailed. Raoul's Rules look like a condensed version—but then Raoul's are older.

[45] 1568.—The secretes of the | reuerende Maister Alexis of Piemount: contayning excel- | lent remedies agaynste diuers dyseases, woundes, and | other accidentes, with the maner to make dystillations, parfumes, | confitures, dyings, colours, fusions, and meltings. A worke | wel approued, very profitable and necessary for euery man. | Newly corrected and amended, and also somewhat | enlarged in certayne places which wanted in | the first edition. Translated out of | French into Englishe, by | William Warde. | [Device] | Imprinted at London, By | Henry Bynnemann, for Iohn Wight. | Anno Domini. 1568. | Small 4°.

[46] 1570. [Des wolerfarnen Herren | Alexij Pedemontani, von den Secreten, | oder Künsten, . . .] | [Colophon] | Getruckt zu Basel bey | Peter Perna, da man zalt nach Christi | geburt M. D. LXX. | Small 8°.

[47] 1573. Kunstbuch | des Wolerfar— | nen Herren Alexij Pede— | montani vō mancherley nutz— | lichen vnnd bewerten Secreten | oder Kunsten, jetz neuwlich ausz Wel— | scher vnnd Lateinischer sprachinn | Teutsch gebracht, durch | Doctor Hansz Jacob Wecker, Statt | Artzet zu Colmar. | [Vignette] | Mit Keys. Maiest. gnad vnnd freyheit, inn | sechs jaren nicht nachzutrucken. | ——M. D. LXXIIJ. | Small 8°.

Contains six books. A simple reprint of the earlier 1570 edition.

[48] 1573 St. John's Coll. Cambridge. | Kunstbuch | Des Wolerfar— | nen, herren Alexij Pedemonta— | ni, von mancherleyen nutzlichen vnd | bewerten Secreten oder | Künsten, | Der Ander theil. | Jetzt neuwlich verteutscht, durch | Doctor Hansz Jacob Wecker, Statt Artzet zu Colmar, | [Vignette, as before] | Mit Keys. Maiest. gnad vund freyheit, inn sechs jaren nicht nachzutrucken. | —— | M. D. LXXIII. | Small 8°.

This second part contains the most of Part II (English trans. 1614-15) and a good deal of Part III (Italian, 1568) but Wecker has added receipts either of his own, or taken from other sources. It contains the Physic of the Months.

A certain amount appears also in the French translation (1614) Part II Books I—v.

[49] 1573. D. ALEXIE | PEDEMONTANI | DE SECRETIS LI— | *BRI SEPTM.* | *A IOAN. IACOBO VECKERO Doctore Medico,* | *ex Italico sermone in Latinum con*— | *uersi, & multis bonis Secretis aucti, diligentiusq ca* | —*stigati,* | *ACCESSIT eiusdem Vueckeri opera, octa*— | *uus de artificiosis uinis liber.* | *EDITIO TERTIA.* | *BASILEÆ* APUD PETRVM PERNAM | M. D. LXXIII. Small 8°.

This seems to be a simple reprint of the 1563 edition.

[50] 1573. B.M. 7944 a 25. LES | SECRETS DV SEIGNEVR ALEXIS PIEMON- | TOIS, DIVISEZ EN DEVX PAR- | ties, & chacune d'icelles en six liures: Et aug- | mentez d'un liure de distillation, auec fi- | gures des fourneaux propre à ce: nō | par cy deuant imprimé. | AVEC | LA TROISIESME PARTIE DES receptes | de diuers autheurs, toutes vien experi- | mentées & aprouuées: Cōtinuant les li- | ures dudict Seigneur Alexis. | PLUS | L'ECOIATRIE, LAQVELLE | contient grans secretz sous choses domestiques | & de nul pris, recueillie dés liures | de Dioscoride, Galen, | & autres. | PAR CHRISTOFLE LAN- | dré, docteur en Medecine, & Lecteur de feu | de bonne memoire Monseigneur le | Duc d'Orleans. | AVEC VNE TABLE GENE- | rale de toutes matieres cōtenues | audict liure. | A PARIS, | De l'Imprimerie de Hierosme de Marnef, | & Guillaume Cauellat, au mont S. Hi- | laire, à l'enseige [*sic*] du Pelican. | 1573.

The Kunstbüchlein receipts pp. 760—846.

[51] B.M. 545, e. 3. Artzney Buch. | Des Wolgelehrten | Herren Alexij Pedemontani gar nach | allerhandt Kranckheiten zu Curie- | ren fast dienstlich. | Ausz Welscher vnd Lateinischer sprach | in Teutsch gebracht, vnnd ordenlich [*sic*] | zūsammen verfasset. | Durch | Hans Jacob Wecker Physicum | zu Colmar | Getruckt zu Basel, bey | Peter Perna. | Mit Rö. Key. May. freyheit nicht nachzutrucken | M. D. LXXV. | Small 4°.

This is not a translation of Alessio, but a re-arrangement in three books, under different *diseases*. It is purely medical, and different from the Kunstbuch.

[52] 1576. LES | SECRETS DV | SEIGNEVR ALEXIS PIEMON- | TOIS, DIVISEZ EN DEVX PAR- | ties, & chacune d'icelles ex six liures: Et aug- | mentez d'un liure de distillatiōs, auec fig- | fures des fourneaux propre à ce: nō | par cy deuant imprimé. | AVEC | LA TROISIME PARTIE DES | receptes de diuers autheurs, toutes bien experi- | mentées & aprouuées: Cōtinuant les li- | ures dudict Seigneur Alexis. | A PARIS, | De l'Imprimerie de Hierosme de Marnef, | & Guillaume Cauellat, au mont S. Hi- | laire, à l'enseige du Pelican. | 1576. | 16°.

[53] 1578. *A verye excellent and pro-* | fitable Booke conteyning sixe | **hundred foure score and odde ex-** | perienced Medicines, appertayning vn | **to Phisicke and Surgerie, long time** | *practysed of the expert and reuerende Mayster* | Alexis, which he termeth the fourth and finall | **Booke of his secretes and which in his latter** | **dayes he did publishe vnto a vniuersall be-** | **nefite, hauing vnto that time reserued** | **it onely vnto himselfe, as a most** | **pryuate and precious** | **treasure.** | Translated out of Italian into Eng- | lishes, by Richard Androse. | Humilia la anima tua a Dio: a gran signori | fa riuerentia, & a gridar del pouero inclina | le orecchie. | ℭ. Imprinted at London | by John Wyght. | 1578. | Small 4°.

[54] 1580. Biblioteca Nazionale, Florence. | DE' | SECRETI DEL REVERENDO | DON ALESSIO | PIEMONTESE | PARTE PRIMA. | DI | Nuouo riueduta, corretta, & ampliata in più | loughi. | Con la Tauola per trouare le ricette

con ogni | comodità. | [Device of fortune on a Dolphin with a Sail, & the Nords above: NON BIS] | In VENETIA Appresso Alesandro gardane. | M.D. LXXX. | 8vo.

Then the Second Part:—De' | Secreti Del | Reverendo | Don Alessio | Piemontese | Parte Secvnda. | Di | Nuouo rimeduta, corretta, & ampliata in più | luoghi. | Con la Tauola per trouar le ricette con ogni | commodità. | [Device] | In Venetia Appresso Alessandro Gardane. | M. D. LXXX. | 8vo.

Part III:—De' | Secreti Del | Reverendo | Donno Alessio | Piemontese | Parte Terza. | Di | Nuouo rimeduta, corretta, & ampliata in più | luoghi. | Con la Tauola per trouare le ricette con ogni | commodità. | [Device as before] | In Venetia Appresso Alexandro gardane. | M. D. LXXX. | 8vo.

[55] 1595. St. Genevieve. Bodl. Mortara Adds. Sept. 21, 1891 PRIMA PARTE | DE' SECRETI | DEL REVEREN. DONNO | ALESSIO PIEMONTESE. | NVOVAMENTE RISTAMPATO, | Et con somma diligentia corretto. | Et di nuouo aggiontoui la quarta parte, con le sue | Tanola per ordine accommodate. | Con licentia de' Superiori. | [Vignette] | IN VENETIA, | Appresso Oliuier de' Alberti. | M. D. XCV. Sm. 8°.

[56] 1595. The Secrets of the reuerend | Maister Alexis of Piemont, con- | taining excellent remedies against diuerse | diseases, wounds, and other accidents, with | the maner to make Distillations, Par- | fumes, Confitures, Dyings, Colours, Fu- | sions, and Meltings. A worke well ap- | proued, verie necessarie for | euerie man. | Newly corrected and amended, and also somewhat inlarged in certaine places, | which wanted in the first edition. | Translated out of French into English by | William Ward. | [Device] | Imprinted at London by Peter Short, for | Thomas Wight. | 1595. | Small 4°.

[57] 1603. PRIMA PARTE | DE' SECRETI | DEL R. D. ALESSIO | PIEMONTESE. | NVOVAMENTE | RISTAMPATO, | & con somma diligentia | corretto. | *Et di nuouo aggiuntoui la* | *quarta parte,* | *con le sue Tomole per ordine* | *accommodate.* | CON LICENTIA DE' SUPERIORI. | [Vignette] | IN VENETIA, M D CIII. | Appresso Lucio Spineda. | 8vo.

[58] 1603. DELLA QVARTA | ET VLTIMA PARTE | DE' SECRETI | DEL R. D. ALESSIO | PIEMONTESE. | *Nella quale si contengono diuersi medicamenti, veri, & approuati, tolti tutti da' principali* | *Auttori della Medicina.* | NVOVAMENTI DATI | in luce à beneficio di ciascuno. | CON LA TAVOLA DA | *trouare i remedi conogni facilità* | [Vignette.] | IN VENETIA, M D C III. | Appresso Lucio Spineda. | 8vo.

[59] 1603. D. Alexii | Pedemontani | De Secretis | Libri Septem: | A Ioan. Iacobo | Weckero, Doctore Medico, ex | Italico sermone in Latinum con- | uersi, & multis bonis Secretis | aucti diligentiusq; ca- | stigati. | Accessit euisdem Vueckeri opera, octauus | de artificiosis vinis liber. | Editio Qvarta. | Basileæ, | Sumptibus Lvdovici Künig. | CIↃ IↃ CIII. | Small 8vo.

[60] 1614. Les | Secrets | Dv Seignevr | Alexis Piemon- | tois. | Reueu, corrigé, & augmenté d'vne | infinité de rares Secrets. | Derniere Edition. | A Roven, | De l'Imprimerie de Robert De | Rovves, sus la Renelle, pres | les Lyons couronnez. | 1614. | 16°.

In the Bibl. St. Genevieve copy.

[61] 1615. The | Secrets | Of | ALEXIS: | CONTAINING MANY | Excellent Remedies | AGAINST DIVERS DISEASES, | wounds and other Accidents. | With the maner to make | Distillations, | Parfumes, | Confitures, | Dyings, | Colours, | Fusions, | and | Meltings. | A worke well

approued, very necessarie | for euery man. | Newly corected and amended, and also | somewhat more enlarged in certain places, | which wanted in the former | Editions. | LONDON, | Printed by WILLIAM STANSBY for Richard Meighen | Small 4°.

[62] 1616. B.M. 1038. c. 30. Kunstbuch | Des Wolerfar- | nen Herren Alexij Pede- | montani, von mancherleyen nutz- | lichen vnnd bewerten Secreten oder Kün- | sten, jetzt newlich ausz Welscher vnd Lateini- | scher sprach ins Teutsch | gebracht, | durch | Doctor Hansz Jacob Wecker, | Stattartzet zu Colmar. | Mit Keys: Maiest. Gnad vnd Freyheit, | in sechs jahren nicht nach zu | trucken. | Getruckt zu Basel, In verlegung | Ludwig Königs. | M DC XVI. | 8vo.

Second Part, with the following title. Kunstbuch | Des Wolerfar- | nen Herren Alexij Pede- | montani, von mancherleyen nutz- | lichen vnd bewerten Secreten | oder Künsten, | Der Ander Theil. | Verteuscht [*sic*] durch | Doctor Hansz Jacob Wecker, Statt- | artzet zu Colmar. | Mit Keys. Maiest. Gnad vnd Freyheit, | in sechs jahren nicht nach zu | trucken. | Getruckt zu Basel. In verlegung | Ludwig Königs. | M DC XVI. | 8vo.

Printed as an addition is Wecker's own tract about distilled waters, oils, &c.

[63] 1616. Kunstbuch des Wolerfarnen Herren Alexii Pedemontani, | con mancherley nutzlichen und bewerten secreten oder Kun- | sten, jetzt newlich ausz Welscher und Lateinischer | Sprach in' + Teutsch gebracht durch Hansz Jacob Wecker. | Basel. 1616. |

[64] 1639. C. U. L. De' Secreti | Del R. D. Alessio Piemontese. | Nvovamente Ristampati. | & consomma diligentia corretti. | Prima Parte. | El di nuouo Aggiuntoui la quarta Parte | con le sue Janole per ordine | accommodate. | [Device] | In Venetia, M.DC.XXXIX. | Appresso Ghirardo Imberti. | 8vo.

. . . | Parte Seconda. | Con La Tavola Da | trouare i remedi con ogni facilità. | [Device as above] | In Venetia, M DC XXXIX. | Appresso Ghirardo Imberti. | 8vo.

. . . | Parte Qvarta, & vltima. | . . . [as in Parts two and three.] | 8vo.

[65] 1627. Les | Secrets | Dv Seignevr | Alexis Piemon-tois. | Reueu, corrigé, & augmenté d'une infi- | nité de rares Secrets. | Derniere Edition. | A Roven, | Par David Gevffroy, ruë des | Cordeliers joignant S. Pierre. | M. DC. XXVII. | 16mo.

The Kunstbüchlein receipts pp. 760-846.

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Printed in modern black letter, but the title, preface, headings of the chapters, the tables and headlines are in roman.

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[68] 1691. B. M. 7321 aaaa 5. LES | SECRETS | DU | SEIGNEUR | ALEXIS | PIE'MONTOIS. | Revû & augmenté d'une infinité de | rares Secrets. | A ROUEN, | Chez JEAN-BAPTISTE BESONGNE, | ruë Eeuyere, vis-à-vis la petite ruë [*sic*] S. Jean, | au Soleil Royal. | M. DC. XCI. | 8vo. |

[69] 1691. Les | Secrets | Du | Seigneur | Alexis | Pie'montois. | Revû & augmenté d'une infinite de | rares Secrets. | A Rouen, | Chez Jacques De La Motte, Imprimeur- | Libraire, rnë du Bec, au grand Livre Couronne. | M. DC. XCI. | 8vo.

This edition does not contain Alexis's account of himself, and of the origin of the book.

Section of Comparative Medicine.

President:—Mr. G. H. WOOLDRIDGE, F.R.C.V.S.

[*October* 22, 1930.]

Avertin Narcosis in the Small Domestic Animals.

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THE value of colonic narcosis has long been recognized in veterinary practice, and attempts have been made to use the older methods in a manner similar to that adopted in man. We have used the rectal ether method of Gwathmey, but have not obtained good results. In America Beckman [5] has recorded success in dogs from the introduction into the colon of a 75-25 olive oil-ether mixture, after having narcotized the animal by the subcutaneous injection of comparatively large doses of morphine (0·019 grm. per kg. or 1½ gr. per 20 lb.). Our experience of this method has not been satisfactory. Later we adopted the preparation used in the human subject by Basil Hughes [3], and with this we were able to produce anæsthesia. The results were too uncertain for the method to be of any practical value. The onset of narcosis was too slow and the animal usually ejected the liquid before narcosis was attained. It was also attended by excitement.

We greatly needed a safe and reliable narcotic for the cat, and lately have been using avertin anæsthesia. This animal is particularly resistant to the action of most of the recognized narcotics. Morphine is useless, giving rise to excitation and delirium. Agents such as chloral hydrate, paraldehyde and the barbital group, are most uncertain, and although urethane is used by physiologists, we have no knowledge as to its consistency or safety. Thus, for narcosis in the cat, we had been compelled to use chloroform or ether, or a mixture of these, by inhalation. Inhalation anæsthesia is by no means free from risk, nor is administration a simple procedure. The period of excitement tends to be greatly exaggerated, particularly as the animal fears—and resists vigorously—compulsion to inhale a strange and pungent vapour. One of the most striking features of avertin narcosis is absence of violent struggling during induction.

These notes on the use of avertin in animals are the result of our experience in 110 cases: 70 in the cat, 37 in the dog, and 3 in the horse, the animals having been presented for treatment at the Poor Out-patients' Department at the Royal Veterinary College. They comprise animals of all ages and sizes.

The cat.—I will deal firstly with the cat. It is with this animal that we have done most work. It is the species in which a rectal narcotic is most indicated, and it is also the one in which we have obtained the most consistent results from avertin. Our first concern was dosage. It had already been established that for man a safe and effective dose was 0·1 grm. per kg. body weight [1, 2], and with this we commenced. It produced, however, only slight narcosis, and so we increased it until we arrived at the conclusion that for comparatively healthy cats a dosage of 0·3 per grm. provoked narcosis which in 60% of cases amounted to general anæsthesia and in the remaining 40% produced a narcosis far more profound than

any other narcotic at our disposal, but one in which sensation was not completely lost. In these cases, we have found the induction of complete anæsthesia by inhalation to be a simple and safe procedure. The method of computing the dose by body weight is the best at our disposal, but we hasten to add that disease, age, etc., must be taken into consideration. Young animals are considerably less susceptible than adults, and the 40% mentioned previously practically all occurred in animals under 9 months old.

It may be of interest to mention here what these doses actually are. The average adult cat weighs from 8 to 12 lb. (3·7 to 5·4 kg.) and the dose of avertin is from 1 to 1·5 c.c. The smallest dose we have used is 0·35 c.c. (6 minims) for animal weighing $2\frac{3}{4}$ lb. and the largest 2 c.c. for one weighing 15 lb. The total amount of the injection varies from 12 to 60 c.c. ($\frac{1}{2}$ to $2\frac{1}{2}$ oz.).

Of the cats dealt with we have had three deaths attributable to avertin.

The injection is prepared in the manner recommended by the makers and the technique of administration will be demonstrated to you.[1] We do not prepare the subject in any way. It must be borne in mind that when dealing with animals of a highly nervous nature, such as the cat, the less interference and restraint used, the better the results.

Although the congo red test for acidity is said to be obligatory, we have never found avertin break down during preparation. In 3% solution it is entirely without irritant effect upon the rectal mucosa and never produces straining. It is rapidly absorbed, and evidence of muscular relaxation occurs from two to three minutes after injection, whilst the onset of narcosis generally occurs in from five to eight minutes. It is usually preceded by a slight phase of involuntary excitement, indicated by a few tetanic spasms of the limbs and back. In exceptional cases the onset of narcosis is extremely rapid and entirely without evidence of excitement; in fact, we have had cases in which general anæsthesia was present 45 seconds after the completion of the injection.

I have previously referred to the fact that once absorption has occurred, all evidence of struggling is lost; in fact, throughout, the sensation appears to be a delightful one. Quite frequently one finds an animal purring away in a condition resembling natural sleep. Narcosis reaches its maximum depth in about fifteen minutes and persists thus for from one to two hours. This is followed by a period of sleep for some twelve hours and locomotor inco-ordination is often still present after twenty-four hours. Recovery is not accompanied by any sickness or nausea, in fact food is quickly taken.

In safe anæsthesia, respirations become slower and shallower, but remain regular, usually from twenty to thirty to the minute. The pulse is accelerated and may be 200 or more. A noticeable action upon the circulatory system is a marked dilatation of the peripheral tissues. The skin becomes suffused with blood and a marked warmth of the ears and extremities is felt. The tip of the nose (if unpigmented) and the gums become bright pink. To avoid loss of heat by radiation we make a practice of keeping the animal warm. The action upon the pupil is worthy of mention. In light anæsthesia, when light and corneal reflexes are present, there appears to be little or no effect upon the pupil, but in profound anæsthesia and when reflexes are lost, the pupil contracts and becomes a mere slit. This is considered by some to be evidence of toxicity.

The dog.—The action of avertin in this animal presents some striking differences. Firstly, the dose necessary to produce narcosis is considerably greater, varying from 0·4 to 0·6 c.c. per kg. body weight. In large dogs the actual dosage necessary is greater than that required for man. We have given as much as 10 c.c. Secondly, the narcosis produced is by no means constant, varying from a transient stupor to a profound general anæsthesia. Thirdly, the duration of effect is always short, as compared with that in the cat. The same dose given to similar animals under

[1] A demonstration followed the reading of the paper.

similar conditions will in some cases give rise to general anæsthesia which may last for several hours, whilst in others its effect may only last for twenty minutes or even less. Fourthly, the therapeutic margin is smaller and a dose capable of producing serviceable narcosis may cause respiratory failure. Finally, recovery from the effects of the drug is extremely rapid. There is never a period of hours during which the animal is in a condition of sleep. General anæsthesia is followed in the course of fifteen to thirty minutes by complete recovery.

As toxicity, it has been previously mentioned that, whilst the best method of computing the dose is by body weight, it is far from foolproof. Allowance must be made for age, disease, infirmity, etc., and this can only come as the result of experience with the drug. Any agent having such a profound effect upon the central nervous system must be associated with danger.

Clinical experience has taught us that old age, chronic suppuration and chronic kidney disease are conditions likely to give rise to collapse during avertin narcosis. In this connection it is of interest to notice that C. Bless [4] has shown that reduction in the calcium and natrium content of the blood increases the toxicity of avertin and reduces the quantity necessary to produce narcosis. It has been shown that, as with other poisons, the protective rôle of the liver is proportional to its glycogen content, so that with fasting animals the dose must be reduced.

I will not attempt to deal with the fate of avertin. It is held that the kidneys are the chief means of excretion, but that excretion is slow and that cumulation may occur if a second dosage is given too soon [6]. Our experience is that whilst this is true in the case of a cat, it is not so in the dog. In this animal we find that excretion is rapid. We have given a four-months' old puppy a 0·4 grm. dosage, which gave rise to a transient narcosis. In one hour's time this was followed by a 0·5 grm. dose and again only transient narcosis occurred. A 0·9 grm. dosage given at one time would probably have proved fatal.

In cases of poisoning collapse occurs early, usually from 5 to 10 minutes after injection. There is a notable change in respirations. A deep inspiratory movement is followed by a quivering of the abdominal muscles, after which all respiratory movement may cease. Sometimes the Cheyne-Stokes type of respiration is observed. The heart always continues to beat for from two to ten minutes after respiratory movements cease. Prompt antidotal treatment should immediately be given.

A case will serve to illustrate this:—

Three-years old male Pekingese dog, suffering from a necrotic neoplasm the size of an egg, involving upper lip and gums. Weight 4 kg. (9 lb.), dosage 0·4 grm. = 1·6 c.c. In one minute general anæsthesia. At 1½ min. respirations ceased. Heart beating slowly and irregularly. Adrenalin 0·5 c.c. given intraperitoneally. Artificial respiration commenced. Normal saline 15 c.c., subcutaneously 50 c.c. per rectum. Fifteen minutes: breathing recommenced. Thirty minutes: sensation returning. One hour: complete consciousness. Twenty-four hours: normal as regards avertin.

We have had, in animals, six deaths definitely attributable to avertin, three in the cat and three in the dog. In four there was extensive suppuration, in one, advanced chronic nephritis. In the sixth animal, a cat, no predisposing cause could be found.

Conclusions.—For the cat, avertin, per rectum, in a dosage of 0·3 grm. per kg. body weight is, in healthy animals, a consistent and safe narcotic. In adults this narcosis is usually sufficiently profound to be classed as general anæsthesia. In young animals, however, narcosis alone is the general rule, so that for completion of anæsthesia, a little chloroform or ether by inhalation is necessary.

Administration is easy. The induction of narcosis is not accompanied by any violent struggling, and, although the influence of the drug persists for from twelve to twenty-four hours, it is not associated with any nausea or vomiting.

It will prove a very valuable addition to the agents at our command for provoking narcosis in the cat.

For the dog it is uncertain. The therapeutic margin is small, and thus considerable experience is necessary in computing the dose. Whilst for operations about the head it has considerable advantages over most of the other agents at our disposal, for general surgical work it is inferior to morphine as a narcotic.

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In reply to queries in discussion on the paper, the author said: We have used avertin on three occasions in the horse. Expense prohibits its use rectally, and so we have given it intravenously. 10 c.c. given in 300 c.c. of distilled water by the jugular vein caused a 10-cwt. draught mare to fall to the ground anæsthetized in two minutes. Narcosis persisted for eight minutes. Whilst transient anæsthesia of this nature may be serviceable for such operations as castration, for more prolonged anæsthesia chloroform by inhalation will be necessary. In this respect the drug is inferior to chloral hydrate for the horse.

In cases of collapse, the antidotal measures adopted have been the intraperitoneal injection of adrenaline with a view to causing a rapid rise in blood-pressure, and thus serving to stimulate the respiratory centre and the subcutaneous and rectal injection of normal saline, combined, of course, with continuous artificial respiration. In this connection, in view of the findings of Bless, calcium gluconate might be useful.

Several operators have referred to the variation in the dog, as compared with the cat. It would appear that the dog is capable of breaking down and excreting avertin much more quickly than is the cat.

We do not find the persistence of narcosis for twenty-four hours a disadvantage, in fact in many cases, particularly those of abdominal operations, it is a distinct advantage to have the animal comatose for twenty-hours immediately afterwards.

United Services Section.

President—Surgeon Captain SHELDON F. DUDLEY, O.B.E., R.N.

[*October* 13, 1930.]

PRESIDENT'S ADDRESS.

Some Aspects of Specialization and Research in the Services.

By SHELDON F. DUDLEY, O.B.E., R.N.

IT is becoming more and more obvious that no one man can master more than a fraction of the accumulated knowledge, or have time to acquire the technical ability necessary for the efficient practice of more than one or two of the numerous subdivisions of applied medical science. Specialization or division of labour solves the problem to some extent. And the time seems near when the general practitioner will be the most important specialist of all, with the chief function of informing patients to which experts to go. To perform this duty adequately he will require a far wider knowledge than anyone who specializes on a single organ of the body. This may be feasible ashore, in areas where the population can support a team of medical men, but in the Services the all-round medical man is still required, especially in ships and isolated districts with small populations.

Of late years the practice and study of medicine has been developing more as a science than as an art. The pose of confident omnipotence formerly typical of the family doctor has largely been replaced by the diffidence of the student of nature, and the value and necessity of medical research are becoming recognized. As it has been my fortune to have been engaged about equally in general, special and laboratory practice in the Royal Navy, I presume to make a few remarks on these important subjects.

Sir Thomas Lewis [1] recently pointed out that medicine falls naturally into two main divisions—curative and progressive. The former is practically the craft of applied medicine, the latter is research. We can further divide both of these two main divisions into individual and collective medicine—general practice and public health. Public Health can be divided into curative preventive medicine, or herd-treatment, and progressive preventive medicine, or herd-pathology. It must be clearly understood there are no watertight bulkheads between these departments of medicine. Anyone who administers a remedy to a patient practises progressive medicine in so far as he notes the sequence of events in a certain type of subject under a specific set of conditions. Lewis draws attention to the divergencies in the method of approach towards pure curative and pure progressive medicine. In curative medicine diagnosis is the main end-point whose object is to recognize the known in order to administer the correct established remedy, if any. The worker in progressive medicine has no interest in the known, except as a starting-point to reach

out into the unknown. Secondly the whole duty of the practitioner of curative, and preventive medicine is to do the best for the individual, or the herd, with the knowledge and material at his disposal. To the scientific investigator the individual or community is of no importance or interest, unless as material to help the progress of scientific medicine. In so far as he is allowed any humanitarian interests at all, the researcher works largely for the future, and is glad if during his lifetime any of his work should prove useful in presenting applied medicine with new methods of diagnosis or treatment. Thirdly, there is the difference in the mental attitude of the curative and progressive worker. There is no doubt that from both the patient's and the doctor's point of view, telling the literal truth to patients is incompatible with sound medical therapeutics. If we always confessed to the truth that is in us, we should often have to say to our patient, "I do not know what is the matter, I do not believe the treatment I am ordering will do you any good, but hope it will not do you any harm, and make you more comfortable," and, paradoxical as it may seem, the more widely read a doctor is, the more often he finds himself in this position. Pedantic honesty in a practitioner of curative medicine is a selfish luxury and bad practice, and may account for some of the bad reputation Service medicine used to have among certain ignorant or misinformed circles. Francis Bacon has said: "To pronounce disease incurable is to establish negligence and carelessness as it were by law, and screen ignorance from reproval." And, however much a practitioner realizes his ignorance, it is an essential part of therapeutics to deceive the patient as to the fact. More, the fact itself should never be an excuse for the neglect of patients, but a continual spur to find out what little is really known, in order to place it at his patient's disposal, and to make certain he does not miss one of the many conditions in which he can help Nature, or that he does not destroy the only remedy which is helpful in every malady—confidence in the doctor. On the other side, progressive medicine is science, and science is the definition of truth. As Lewis [1] says:—

> "The very essence of daily observation and thought in scientific work is the continual effort to discriminate as closely as possible between what is true and what is less true or actually false. The standard of truth attained by constant and deliberate cultivation among scientific men in their work greatly transcends that in any other sphere of human thought. It is a standard that allows no statement to pass without full qualification, without full display of its limitations. It is a standard essential to progressive work but one highly inconvenient and even obstructive in the practice of everyday life."

The qualities required for the pursuit of progressive and curative medicine are so divergent as to make it seem improbable they can be successfully blended in one individual. Nevertheless, the plasticity of the mind is such that it is possible, and I speak from experience, to enter a ward, be convinced that a case is one of influenza, prescribe aspirin with certainty that it will be efficacious, and confidently assure the patient that he will be well in a week. Five minutes later the practising investigator is in his laboratory facing what appears to be the only interpretation of drastically controlled experiment, and becomes a flabby mass of indecision and doubt, After all, the difference in mental attitude is only due to a common psychological mechanism, a mixture of dissociation and repression which, unless we are critically introspective at the time, passes without notice, and which many happy men never discover at all.

I think many men can practise both the curative and progressive branches of medicine with success; in fact the long list of practitioners of applied medicine who have made notable contributions to progress indicates that this must be so. However, while certain types of medical research are more easy and fruitful if the investigator is actively practising administrative or curative medicine at the same time, yet the converse does not hold good, and the essentially critical attitude of the scientific investigator does interfere with his ability in the art of managing and treating patients, because it is bound to undermine his confidence in much of his daily work.

In fact we all know the type of consultant whose extensive knowledge so fills him with hesitancy and doubt that he is of little use to the general practitioner who hopes for a definite opinion. Most of us can remember the happy state of mind we were in at the time we qualified. Every statement in our textbook, or uttered by our teachers, was an unimpeachable fact. Our medical education largely consisted of memorizing a medley of facts, theories, opinions and legends, giving to them all an almost equal amount of credence. The relative probability of the truth or falsity of any statement was rarely indicated. To some extent this may have been unavoidable, seeing the mass of detail a medical student must of necessity absorb to practise the profession of applied medicine. One sometimes feels that the medical practitioner should endeavour to remain in this state of mind, by never reading anything but the last edition of his favourite textbook, and believing that every word in it is the literal truth. Many first-class practitioners do, I think, remain in a frame of mind approaching to this, and they and their patients are happier for it. And, as probably more than 90% of men never recant from the religious, political, or medical creed in which they were brought up, I presume that the majority of practitioners are consciously honest, while unconsciously deceiving themselves and their patients.

In addition to the natural divisions of medicine into curative, progressive, individual, and collective, there is the more artificial subdivisions into "specialisms." Keith [2] shows how this specialization is the result of the "inexorable law of evolution" which applies to medical practitioners as much as to any other group of organisms. As a result of the growth of medical knowledge, the profession has of necessity to split up into an ever increasing number of specialists. The advantages of specialization are evident, but there are also disadvantages. The highly specialized doctor, just as any other highly specialized animal, is closely adapted to only one type of environment, in which he far outshines the more plastic general practitioner, who is, however, much more at home in all other types of medical environment. Under the present system of medical organization and education the practitioner generally specializes too early. In unconscious defence of his ignorance of things outside his own department, he sometimes develops an air of superiority over the more generalized doctor, who has to be a wider-read and more adaptable individual or go under. Again, the breaking up of the medical profession into sub-herds, often of differing ideals and customs, has led to a certain amount of friction between the groups, which may hinder progress in some directions while advancing it in others by stimulating healthy rivalry. The following purposely overdrawn incident will show what I mean. When I was doing both ward and laboratory work, an eminent pathologist visited me in the latter environment. I had to excuse myself to go and see an urgent case. When he realized what I was going to do he said, "Good Lord! man, you do not tell me you actually have to go into the wards and open people's bowels." I shall never forget his tone of pity and reproach; I felt I had been thrust out of his herd of pathologists. I was a pariah—a clinician.

In certain subjects early specialization seems actually to induce pride in ignorance of general medicine and surgery. The following episode illustrates such a tendency, which should always be discouraged while the subject's mind is still plastic enough to receive impressions. At one of the naval hospitals early in the war, a recently qualified youngster, who had begun to specialize, joined up as a temporary surgeon lieutenant. He was rightly made specialist in his own subject, but in accordance with an excellent naval custom he was also expected to do some general duties and keep days on. Learning this, he "fell in" to see the principal medical officer, to whom he explained that it was dangerous for him to keep a day on, as he might miss an "acute abdomen" or a case of infectious disease—because he was a "specialist." Much to his colleagues' disgust, he got away with it, and was relieved from days on. I may add that if I had been P.M.O. he would have kept days on and stopped on, under his general practitioner colleagues, until he felt that he could

spot appendicitis or mumps with the degree of certainty required of the general practitioner. These little failings can be winked at ashore, where a much greater subdivision of labour is possible and desirable than at sea, but they need not be encouraged in the Services where, under the close conditions of living, they are less tolerable. In the Navy there is not the work for many whole-time specialists, because there are not enough special cases. Therefore we can avoid the narrowing effect of specialization, while retaining much of its usefulness, by refusing to let medical officers specialize officially before attaining their "half stripe" and sticking to the excellent custom of making specialist medical officers keep *au fait* with general medicine, and with administrative duties. Another excellent naval custom, which I hope will never be dropped, is that all surgeon commanders should serve a commission at sea before further promotion. Among certain naval medical specialists and bureaucrats I know this custom is unpopular, but for the good of the Service and senior three-stripe officers themselves, I hope the rule will continue to be rigorously enforced, especially with regard to those officers who specialize in administration. Many hospital doctors and administrators, who have been long ashore, forget how rapidly the Navy has changed and is changing, and many also seem to forget, or perhaps never knew, that they are the servants of a sea-going Royal Navy. The specialist the Royal Navy wants is a man with at least the average knowledge of general medicine and surgery with an extra training in some speciality in addition thereto, but not in lieu thereof. Moreover, if the Service is to get the best results from its medical experts, they must be familiar at first hand with the conditions of life and duty in ocean-going submarines' and triple 16 in. gun-turrets, as well as in the Victory and the Ark.

It is probably an inexorable psychological law that early and whole time specialization narrows the mental outlook, however plastic the original mind. It is logical to believe that an individual who is continually thinking of one small section of medicine, and only sees patients suffering from one type of illness, cannot help attributing a greater relative importance to his own subject than it is entitled to. Analytical psychology shows how a man's occupation, especially if it is a hobby as well as a livelihood, forms a mental complex which subconsciously influences his judgment and behaviour in completely irrelevant matters. A wise general practitioner is well aware of this, when he is loth to recommend a patient to consult Mr. So-and-So, because he fears that, whether his patient has housemaid's knee or neurasthenia, he will return without tonsils, appendix, or great intestine, according to the surgical complex which subconsciously sways all Mr. So-and-So's actions. The psycho-analyst himself, though he has done invaluable work in showing up the influence of the unconscious mind on the symptoms of patients and on the behaviour of the medical men who treat them, yet seems as prone to this defect as the ordinary man. What may be an example of this tendency in an eminent psychologist is Stoddart's [3] theory of sea-sickness. He says: "The sea is a well-known mother symbol which may be subconsciously associated with the respiratory rise and fall of the mother's breast while the infant is taking food. The rise and fall of a boat during a sea voyage tends to remind certain people of this forgotten situation in an unconscious way, and sea-sickness with its rejection of food is a mode of repressing this infantile memory." Candidly, as a naval surgeon and a dabbler in psychology who has given much thought to sea-sickness, I do not believe that Stoddart's hypothesis rests on a sure enough foundation of fact to recommend that only recruits who were bottle fed as infants should be accepted for the Royal Navy. However, Trotter [4], brilliant psychologist as well as eminent surgeon, warns us that scepticism is not the hall-mark of a scientific mind—that it is just as often "an automatic mental defence against the painful irruption of new ideas." So perhaps I am trying to be funny at the expense of this analogy either because I am insufficiently educated in psychology or because some unconscious influence sways

my judgment. Stoddart himself says that those unfamiliar with psycho-analytical investigations will reject this theory of sea-sickness. However, the illustration holds good even if the hypothesis is right, because I become the example of a mind refusing to believe the truth because some mental resistance prevents my making a logical judgment of the facts, subconsciously using scepticism as a defence against the pain the acceptance of this novel theory would cause me.

Every specialism has its curative and progressive side. Nowadays the exponents of these two divisions tend to divide automatically into clinicians and laboratory workers. This is largely because most, but by no means all, recent progress in clinical medicine, has been secondary to laboratory experiments on animals, and the training and time necessary to acquire the knowledge and technique of modern laboratory work has forced the majority of medical investigators to be whole-time professionals. As Fletcher [5] points out, the day of the amateur is practically over, and, perhaps as a result, the community, used to getting its medical research for nothing, grudges the research worker a fair share of worldly honours and a wage comparable to that of the practising clinician who freely markets the results of his laboratory colleagues' labours. Of course when man is civilized, scientific investigation will become one of the best paid professions, but meanwhile the researcher has to console himself with doing the job he likes best, a blessing given to few in this world. And, although the lack of cash is a real hardship, yet as regards worldly honours I expect most scientific workers agree with Huxley [6] that "The only order of nobility which becomes a philosopher is that rank which he holds in the estimation of his fellow workers, who are the only competent judges in such matters."

The Services, contrary to the general view, offer one of the finest fields for any man with a craving for research, yet not sufficiently enthusiastic to slave for the best part of his life on from £200 to £300 a year in a laboratory ashore. In the Service the would-be researcher will find leisure and opportunity for many types of investigation. In general the Service doctor should look on his research as a hobby and not expect a reward for it. He should remember that his Service duties as a practitioner of preventive and curative medicine always come first; he is neither asked nor paid to research. But in spite of this he will generally find plenty of encouragement from those in authority over him, both medical and executive, and even from his material—the ever-cheerful sailor—if he treats them the right way. Should he be lucky enough to produce results and get advancement thereby, he should regard this as a bonus on the advancement he has otherwise earned. It is noteworthy that in the Services, original work has been recognized and rewarded to an extent which I think is relatively greater than in the civilian profession—a point in which the organization of the fighting Services is ahead of civilian medical practice.

The man with a special bent for research will find plenty of scope for his activities, not only in well-equipped laboratories at the base hospitals ashore, but also in the spacious dispensaries of a modern ship of war, where a man good at devising makeshifts can, if he will, carry out academic laboratory and biological investigations at sea. But this is not the only work I include under research or progressive medicine. The Services offer an ideal field for medico-statistical investigations, for clinical, as opposed to laboratory, research, and for the study of epidemiological problems. Again, there is room for much research in "administration." Also there are still many interesting problems to solve as regards the food, clothing, work, and last, but not least, the psychology of the sailor. Thus progressive medical work in the Services is of a variety to suit anybody's fancy. Except when he is undertaking an investigation by order, the Service researcher is in an enviable position: he works to amuse himself only, he can choose his subject, do as much or little as he likes; it does not matter if, as often is the case, his work leads

nowhere. He can publish or not, but if he thinks his results of Service interest, there are his own journals grateful for copy. In fact the Services are the happy hunting ground and one of the last strongholds of the amateur medical researcher. I use amateur in its literal sense as meaning one who does something for the love of doing it—not one who does something worse than a professional. I write this as an amateur hoping to encourage others to take up a most absorbing hobby. We amateurs spell research with a small r, we do not expect to make any discovery of general importance, we do not even mind if we discover things that have for years been general knowledge to those better informed. We are only amusing ourselves, but if something useful emerges from our pastime so much the better, but that is not the main object of amateurs. Although one may not wholly agree with the professor who at the end of a lifetime spent on some academic research said "Thank God I have never done anything practical," yet, in these sordid times, one cannot but sympathize with his sentiment. There is, however, much investigational work which promises useful results to those who prefer to be practical. There are many problems of little outside general interest, the solution of which would be of value to the Service.

One could ask many conundrums of domestic interest to the Royal Navy, some of which should be answerable if anyone took the trouble to try to find out. There is plenty of progressive work which can be done at sea without any knowledge of out-of-the-way medical literature or special training in laboratory technique.

Now, although the majority of Service research workers are working for their own amusement, if they publish serious results, they should stick to the rules of the game, and make every endeavour to observe the highest standard of literal truth. I shall, therefore, discuss one or two common fallacies and tendencies which spoil much good work and should be avoided in scientific literature. There are two main methods of trying to find the causes of events: observational and experimental. There is really no hard line separating these methods. In the purely observational method, the human agent is passive. He waits for Nature to set the experiment, and records carefully what happens; when Nature has set enough experiments which appear to control each other, the observer makes his deductions. This is a very slow method of progress, as it may be centuries before Nature sets enough of the right experiments or the observer notices the salient points in them to give him the true interpretation he is seeking. In the experimental method the observer is active; he sets his own experiments, which are small imitations of Nature, and numerous control experiments; he alters condition and environment to suit his fancy and may find out in days things that would have taken centuries of passive observation, or could never have been discovered at all, without the observer's active interference. It is only within the last fifty or sixty years, with the advent of the bacteriological era, that experimental pathology has bulked so largely as a separate subject to applied medicine. The experimental method has only limited applications to human beings; but it has been found that the experimental method can be employed in studying disease in animals, and, in a way, it is surprising that the phenomena observed in experimental animals are as often as not found to hold good for man. Moreover, preliminary trials on animals and the experience gained in the technique of experimental science, are allowing a freer and more legitimate application of direct experiment on man himself. The application of the statistical methods, better record keeping, and Lister's gift to surgery, have also given the observational method a fresh lease of life. Before this renaissance of medicine, the observational method had about exhausted itself, and medicine was to a large extent a subject like religion.

The unquestioned acceptance of the pronouncements of authority and of the printed word, however desirable in religion or law, is incompatible with progress in science. No statement of any man, however great and learned, is to be taken as

true just because that man made it. Here we may note the use and importance of references. In discussing scientifically any controversial point it is no use saying that Professor Highbrow said "this is so" unless you say why he said it, or give a reference to the original work from which he came to his conclusion, so that any sceptic can judge the evidence himself. Of course, we have to use and quote authority on any subject when we have not sufficient training or education to judge for ourselves. For example, if I want to make a statement which brings in a point in astronomy I am careful to consult and quote a well-known living authority on the subject, such as, say, Professor Jeans, who, in the opinion of his colleagues, is up to date in all recent astronomical work, and whose conclusion on the point in question is accepted by the majority of astronomers, who are the only group capable of judging the evidence. Provided I have done this, I do not worry if any bacteriologist or surgeon, however eminent, any politician, or journalist, however popular, contradicts me on that point in astronomy, any more than I would worry if the greatest of astronomers criticized my views on the biology of the diphtheria bacillus. On the other hand I am severely shaken, and review my position very carefully, when Dr. J. A. Arkwright does so, because he is one of the greatest living authorities on bacterial variation. In your own subject, where you are capable of weighing the evidence for yourself, you may find what in your opinion is a reliable observation by a practically unknown investigator. Such work you are perfectly at liberty to use in support of your own theories, even if it is contrary to the pronouncements of the leaders of your own sub-group of the scientific herd. These few remarks indicate the proper use of authority in scientific work.

Now a few words as to how it comes about that tradition and authority may hinder progress in knowledge. There has always been a strong instinct in any human herd to worship their dead leaders and respect old herd customs, and the medical profession is no exception. Far be it from me, a naval officer, to decry this tendency in everyday life. Without some such instincts no gregarious species of animal would survive. But because hero-worship is such a deeply ingrained mental character, its influence on scientific work must be carefully watched. We honour the scientific pioneers of the past none the less if we carefully re-examine their work and theories in the light of modern knowledge. And all traditions and herd customs, however admirable, require constant overhauling to ensure that they fit the ever-changing environment. Some present-day writers suggest that there has been little progress in clinical medicine which is not due to the older traditional methods, and that the experimentalists are getting a bit above themselves. Crookshank [7] for example rebukes Harley Street for—"The verbal quackery which allows us to pretend that we are nearer the ultimate understanding of life, death and disease than was Hippocrates." But I think such indictments are scarcely just, for the average modern investigator in ward, theatre, office, and laboratory, approaches his subject in a humbler spirit than the ancients, because he realizes more fully the complexity of biological mechanisms, and admits his complete ignorance of ultimate causes. Although it may savour of blasphemy to say so, what little I have read of the old masters of medicine does not lead me to believe that they were blessed with any greater intelligence than many who are alive to-day. Among those recently dead I would place Pasteur, Lister, Robert Koch, and Manson, on a higher plane of intelligence and attainment than Galen or Sydenham.

One might say that of recent years a large part of progressive clinical medicine has been occupied with the attempt to re-edit our textbooks, and discover what statements are proved, what are probably true and founded on facts, and what are definitely false or mere pious opinions unbased on any accepted facts. As an instance of the unreliability of the older textbooks, I will give the extraordinary statement which used to appear in edition after edition of a popular book on surgery, namely, that a man with a urethral stricture had a corkscrew-shaped stream when he urinated.

As a student, with an elementary knowledge of hydrostatics, I could not believe it, and at the next opportunity I watched two or three stricture patients urinate. Though the volume and initial velocity of the stream were less than normal, it descended in the parabolic curve and continued in the same vertical plane demanded by the first law of motion and the theory of gravitation. This absurdity illustrates a thing the scientific investigator must never let himself do. It might have been legitimate for the originator of the corkscrew hypothesis to have published his opinion as a speculation, and wait for the critic to slaughter him ; but, seeing how easy this opinion was to confirm or refute by observing the next case of stricture, or experimenting with a piece of bent tubing, he would have been wiser to have kept his theory to himself till he could test it himself. Where he committed the " unforgivable sin " against science was to publish a hypothesis as a fact. Of course this is a very gross error, selected to illustrate a principle, but many statements in medical literature which are presented as if they were proven fact, have a low probability of being true. As the great investigator Sherlock Holmes said to that rather unintelligent practitioner Dr. Watson : " It is a capital mistake to theorize before one has data. Insensibly one begins to twist facts to suit theories, instead of theories to suit facts."

A class of work for which our standardized population, living under identical conditions of nutrition and environment and disciplinary control, forms admirable material, is the testing and comparing therapeutic or prophylactic agents. This form of work, unless carefully controlled, is especially liable to the great *post hoc ergo propter hoc* form of fallacy, which permeates and vitiates so much attempted research work in medicine that no excuse is necessary for bringing it up again. It is most interesting to note that we are all perfectly aware that a subsequent event is just as likely to be " in spite of " as " because of " a former event.

Trotter [4] has been so much impressed by the ubiquity of the *post hoc* fallacy that he thinks it the expression of a " characteristic cerebral function," a kind of conditioned reflex. If two events occur frequently enough in fairly close sequence, the mind automatically makes the first the cause of the second, without requiring a logical reason for doing so. There is no doubt that it is a specific criterion of man to be uncomfortable if he cannot supply a cause for any event. Therefore any " cause " becomes better than none. The history of primitive magic, religion and medicine proves this. The real cause not being self-evident, it is easy to substitute a striking or exceptional recent event as a " cause," and thus ease the acute mental anguish of not knowing why, and hence the ubiquity of the *post hoc* fallacy. The absurd lengths to which the " *post hoc* " argument can be carried is best seen in the uneducated and mentally weak. I once asked a reservist his reason for objecting to vaccination. He answered that he was the only survivor out of three brothers, and the only one who had not been vaccinated in infancy. I asked him what his brothers died from. He said that one had been killed in a street accident, and the other had died from pneumonia some fifteen years after the vaccination, which their brother firmly believed was in some way responsible for both their deaths. In therapeutics a host of alleged remedies have been recommended merely on the grounds that patients generally recovered after their administration. And, seeing that many such remedies may have been given as routine for generations and recommended by the highest herd authority, any inquirer, who suggests that the patient may have recovered in spite of them, is generally snubbed for questioning the experience of his betters. But if a man has always given castor oil to his appendix cases what experience can he have of oilless appendicitis ? Because the type and severity of a disease show marked deviations from the average at different times and places, there is practically only one reliable method of testing the value of therapeutic or prophylactic treatment which will eliminate the chances of falling into the *post hoc* trap. This is by taking all the admissions of the class to be treated as they turn up in hospital or sick bay, and treating alternately, one by the new and the next by the old procedure, until a

sufficiently large number of observations have been collected to be of statistical significance. The severity of symptoms, the duration of illness, the mortality, and number of sequelæ in the two groups are then carefully compared. One may note that the smaller the variation in the behaviour of test and control group, the larger will be the number of patients that must be treated before any difference in the two series can be fairly attributed to anything more than luck. There is no better example of the successful application of this method than Leonard Rogers' working out of the treatment of cholera. For many years opium was the routine treatment of cholera, given, I believe, as much in the belief that it increased the patient's chance of recovery as that it made his passing more comfortable. First, by the above method of using alternate admissions as a control series, it was discovered that opium prejudiced a man's chance of recovery. The routine use of opium in the past must have killed thousands of cholera patients who would otherwise have recovered. Subsequently by the use of the same principle, Rogers perfected the hypertonic saline treatment of cholera.

Mackenzie [8] has said that "the principles of modern therapy are the same as those which have been in use for time immemorial—the giving of a remedy whose action we do not understand for a condition of whose nature we are ignorant." Like so many epigrams or aphorisms, this is true according to how literally we interpret it. The optimist would say that salvarsan cures syphilis, that we have a fair idea of how the remedy acts and of the nature of the disease. But the pessimist would be justified in replying that we are not certain if syphilis is ultimately eradicated by salvarsan treatment, and that the scientific description of its action and of the pathogeny of syphilis is still far from complete. But even if the latter view is accepted, salvarsan remains a valuable empiric remedy, because it has been proved according to the strictest of scientific standards that under its influence the early and observable lesions of syphilis will disappear more quickly than if left to themselves. It does not matter in practical medicine whether treatment is empiric or "rational," provided there is a reasonable probability that any beneficial change in the patient, noticed after its exhibition, is due to the remedy and not in spite of it. The difficult question for the practitioner to decide is whether he should use the multitude of drugs or procedures which have been alleged to be remedies merely on the grounds that some patients got well after their use, but which have not been *proved* to do good, and may interfere with a patient's natural tendency to recover. The use of some traditional remedy which appears more or less innocuous is probably justified because of the beneficent effect any *placebo* may produce by suggestion. Nevertheless it is certain that the application of drastic measures in the past, merely because they were the traditional practice, caused much unnecessary suffering and many deaths. But, with the patient and his friends clamouring for one to do something, and with the physician's natural desire to help, the attitude of masterly inactivity is hard to maintain. And I think, even to-day, the conscientious doctor is more prone to over- than under-treat his patients. I can illustrate this principle from the work of Alexander Bryson [8], a distinguished past Medical Director-General of the Navy, a man whose efforts deserve more recognition than they have obtained, a naval surgeon fifty years before his time, to whom the sea-going population owes not a little, if only for his work on the control of yellow fever in the Royal Navy. Bryson, in his book on African Fevers, severely criticizes the methods of treatment in vogue at the time, which consisted of copious bleeding, shaving and blistering the scalp, forced exercise, and, worst of all, mercury pushed to salivation; as much as 120 gr. of calomel were given as a single dose. Bryson points out that, although if a man recovered from yellow fever he ought to have a rapid convalescence, yet the poor wretches who recovered often took months to regain their health, if they were lucky enough not to die from mercurial poisoning. He condemns all these measures as unscientific

and would replace them with absolute rest, cinchona bark and tepid sponging, if indicated. Bryson concludes his indictment of the treatment in vogue in the Navy of his time with a striking paragraph, as true to-day as when written in 1847.

> In most men's minds an over-anxiety begets a disposition to do too much, while, in the absence of a proper reliance in the salutary effects of nature, they impatiently resort to change of measures, which can only tend to harass and disturb the patient.

Truly after reading Bryson's account of the medical practice of his time, one can sympathize with Molière's jibe at the profession, when, in answer to Louis XIV's question, "What does your doctor do for you?" he replied: "Sire, we converse, he orders remedies, I do not take them, and I recover."

I will introduce my last subject with the remarks of another French satirist, Voltaire, who said of a certain physician: "He is a jolly good fellow and knows as much as the rest, and when he sees my teeth are falling out and I am suffering from scurvy, he says I have a scorbutic affection." Words and phrases can often be different and yet mean the same thing, and *vice versa* they can be the same and mean something quite different. Progress in medicine is greatly hindered unless there is no ambiguity about what a writer means. Voltaire's sarcasm illustrates a common failing. Doctors frequently consider that they have made a clever diagnosis, and patients are satisfied if a synonym for a symptom is used. The loose use of the terms rheumatism and neuritis to describe any sort of pains whose ætiology eludes us, is one of the best examples of this deplorable habit. In the Services we can stick out for a more honest standard of diagnosis on our official returns, on which we can surely afford to say: "I do not know." When I first joined the Service it was the custom that every patient must have a diagnosis, and the P.M.O. of my ward had all the tickets put out every Wednesday morning to see that the diagnosis was entered on each ticket. The Service category of P.U.O., though it has been a subject of much sarcasm, has everything to recommend it. It is honest and does not vitiate any conclusions a statistician may draw from sick records when it is strictly adhered to. In a recent paper which Mc Arthur read on indefinite fevers in the Tropics it was pointed out the unravelling of some of the many problems concerning this group was likely to remain impossible so long as many medical practitioners indiscriminately called fevers they could not place with reasonable certainty, enteric, influenza, dengue, malaria, sandfly fever or spirochætosis, according to the fancy of the moment. If progress is to be made in the prevention and treatment of such conditions, or of any condition, the diagnosis must approach certainty, and all doubtful syndromes must be honestly reported as undiagnosable, but carefully described in detail. We can at least be honest on official sick returns if we cannot be so to our patients. There is another way in which words and phrases lead to misunderstanding in medical literature. So many words have changed their meaning or are used by different classes of workers with different meanings. In a paper before this Section [10], I showed how different usages of the words "typhoid" and "enteric" had led to much confusion in medical literature. Another example of a word that causes endless difficulties and conveys a widely different concept in ward and laboratory is "virulence." When such doubtful expressions have to be used, it is well for the writer to define as carefully as he can what he himself means by them. Huxley gives a good example of how the same word with the passage of time comes to mean two different things. The Latin word "spiritus" means "breath," which the ancients considered the most refined part of man. Hence when the alchemists first distilled alcohol from wine they called it spiritus because they considered their distillate the most refined part of wine. Therefore says Huxley [6]: "We use the same word for the soul of man and a glass of gin." The precise meanings of words and phrases are important because one of the most difficult things in the world is to convey in words the exact shade of meaning the author hopes will be read into them.

One has only to teach a little, to write a little, or compare an abstract with an original paper, to realize how easy it is for a student or reader to get hold of a concept which the teacher or author had not the slightest intention of conveying. In attempting original work, if one has to refer to someone else's investigations the original paper must always be consulted. Although abstracts are useful in finding papers bearing on one's own subject, yet in at least a third of the occasions where I have read both abstract and original paper, the author conveyed to me a different shade of meaning from that which he appeared to have transferred to the abstractor. I have seen reviews of my own efforts in which what I thought the important point had been omitted or misinterpreted. This was more likely my fault than the reviewer's, but it serves to demonstrate the real difficulty which many men find in writing unambiguous English. In official paper work I have always found that the most arduous part of my duty was translating the rough draft of a report into the King's English.

The highest possible standard of accuracy in diagnosis combined with a candid confession of inability to label a condition when such a standard is unattainable, is essential if progress in medicine is to be advanced by statistical methods. The environment of the Services is eminently adapted as a field for medico-statistical research, but it is no use pretending a lot of our vital statisticsare as accurate as they might be, chiefly because medical officers will not confess their ignorance. In another address [12] the importance of at least an elementary acquaintance with statistical methods and normal psychology was emphasized, if only to avoid the common arithmetical errors which often vitiate otherwise good work, and in order to realize that the mind is an instrument more sensitive to prejudice and emotion than to logic or fact. The points I have tried to make in this rather disconnected discourse may be summarized in the form of a short catechism which the would-be seeker after truth should always put to himself when confronted with any statement to which he is not personally indifferent. Do I believe—or disbelieve—this thing either because I want to do so, because it is the custom of my herd and my heroes to do so, because of a *post hoc* argument, or because I have misunderstood the author? In this way I think one may reduce to a great extent, though never altogether, the subconscious bias that sways all our thoughts and actions. Finally these remarks were made only as regards Science, who demands of her servants that, irrespective of their own or anyone else's emotions, they eternally struggle to unveil her cold and dispassionate sister Truth. How far it is advisable to carry this principle into everyday life I do not pretend to know. My own irrational reason tells me that suppose it were possible to step out of that phantasy which each of us knows is reality, we should be intolerably miserable, if not mentally dead. Life is only bearable because the mechanisms in our unconscious mind enable all of us, each in his own way, to be certain that black is white. This automatic action defends our consciousness from that merciless goddess Truth, and enables most of us to adapt ourselves fairly comfortably to any herd or environment into which we have been flung by that irresponsible jester Fate. Therefore as regards everyday life I would take the advice of that wonderful old psychologist King Solomon, who says: "*Be not righteous overmuch, neither make thyself overwise. Why shouldest thou destroy thyself?*" (Ecclesiastes vii. 16).

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Section of Balneology and Climatology.

President—Dr. F. G. THOMSON.

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PRESIDENT'S ADDRESS.

The Rôle of Hydrology in Preventive Medicine.

By F. G. THOMSON, M.D.

THE treatment of certain definite diseases by what we now call medical hydrology appears to be one of the oldest forms of practical therapeutics. The fact that certain obviously sick people derived benefit from a course of "baths and waters" has been a matter of common observation from the earliest times. As the result of accumulated experience, and by a process of trial and error, certain particular disorders have come to be generally recognized as specially amenable to this form of treatment. As the knowledge of physiological action of baths and natural medicinal waters has increased, it is becoming more widely realized that such benefits as they are able to confer, lie more in their power to restore to the normal the physiological errors associated with the beginnings of disease, than in their capacity to affect any organic changes already well established.

Most chronic diseases are preceded by a more or less prolonged stage in which errors of function are the main—in many cases, the only—feature, and when we repeat the truism that the earlier the stage of the disorder for which the patient seeks advice, the more likely is a cure, what is really meant is that the benefits resulting from any kind of treatment are mainly confined to the correction of functional disorder. That being the case, it is a question whether we should not, to a certain extent, alter the perspective of our views on the therapeutic value of hydrology, and consider whether in addition to its undoubted value in the relief of certain definite and well established diseases, it should not be regarded as of wider and equally valuable application as a form of preventive medicine.

The present time appears peculiarly suitable for considering any readjustment and fresh orientation of our views on the subject, as we see evidence on every side that the value of hydrology is becoming more widely recognized in quarters where hitherto it would appear to have been of small account. The recent establishment in London, of the Red Cross Clinic for Rheumatic Diseases with its subsidiary stations, the suggestion that similar institutions should be provided in certain provincial towns, the numerous large and well-organized clinics on the same lines in various countries in Northern Europe, and the efforts made on the part of some of the Friendly Societies to provide spa treatment for their members, as an

additional benefit, all testify to the high estimation in which balneology and allied forms of physiotherapy are now held by public authorities, the population generally, and more particularly, those responsible for the welfare of the working classes. Though treatment at such clinics is necessarily deficient in many of the advantages and amenities of treatment at a well-equipped spa, it undoubtedly supplies a want, and as time goes on, and the value of physiotherapy is more generally admitted, there will probably be some similar institution in nearly all large centres.

In view of the increased facilities for treatment that are now, and will be in the future, afforded at these numerous clinics, the question arises whether they may not be even more valuable in the prevention of disease than in its subsequent treatment.

In order to establish the thesis that medical hydrology is of definite value as a form of preventive medicine, it is necessary to consider briefly the physiological effects of this form of therapy, and then inquire how far they are applicable to the restoration of those functional derangements which precede and eventually lead to organic disease. It is neither practicable nor advisable to attempt to give here any detailed account of the physiological principles of hydrology, but in so far as it is possible to epitomize the aims and objects of this form of treatment in a few words, we may say that they are :—

(1) To increase elimination. This is the first and perhaps the most important object. Detoxication and the clearing out of waste products by the suitable action of waters and baths on the bowel, kidneys, and more particularly the skin, must always accompany, if they do not precede, any other hydrological measures.

(2) To train the cutaneous responses to heat and cold, thereby improving the circulation of the blood in the cutaneous areas, and providing for the constant and delicate adjustments necessary to stabilize the heat regulating mechanism of the body.

(3) By irrigating the muscles and subcutaneous tissues with a free and more active circulation of blood, to remove toxins and fatigue products, and with the assistance of massage or other forms of manipulation, to render the tissues more supple and remove stiffness and pain.

(4) Indirectly, by improving the adaptability and elasticity of the peripheral circulation, to adjust the load on the heart, and improve the functional efficiency of the cardiac muscle and cardio-vascular system generally.

(5) By suitable stimulation of sensory nerve-endings in the skin, to improve the delicacy of reactions to heat, cold and other external agencies, improve general nervous "tone" and facilitate the adjustments constantly required between the peripheral and the splanchnic circulation.

(6) By improving the blood-supply and nervous reactions of the tissues and organs generally, coincident with more rapid removal of waste products, to stimulate chemical activity and improve general metabolism.

Though this list of objects may appear at first sight formidably ambitious, I think it may be justly claimed that it is possible to procure many of these various effects. A course of hydrological treatment may be said to constitute a comprehensive, and on the whole, an efficient form of physiological training, and it remains to be seen how far it may be adapted to serve the ends of preventive medicine.

Amongst the important if somewhat insidious factors in the production of chronic diseases, neglect of the skin itself must certainly be seriously considered. The sedentary life imposed on a large proportion of the population, together, in many cases, with the habit of wearing too much clothing, results in a diminution of cutaneous activity, implying a diminution in the excretion of urea, sodium chloride and certain ill-defined toxins, and thereby imposing extra work on the kidneys. The delicate vaso-motor reactions to heat and cold become less responsive, and instead of feeling reasonably comfortable under the varying conditions of a changeable climate, the patient becomes unduly sensitive to heat on the one hand, and, more particularly, to cold on the other. The vaso-motor instabilities which find their expression in

erythromelalgia, cold cyanosed extremities, chilblains, ischæmic spasm, and abnormal sensibility to cold, which occur in certain types of patient, are sufficiently well known to everyone. Whether they are themselves provocative of disease, or whether they are merely the earlier manifestations of some underlying cause, such as chronic infection, which ultimately expresses itself in terms of organic disease, is a debatable point. In the case of the so-called "rheumatic child" there is reason to think, as was ably pointed out by Dr. R. L. J. Llewellyn in his Presidential address to this Section in 1925,[1] that these vaso-motor instabilities are indicative of a "rheumatic diathesis"—a condition which, whether inherited or acquired, lowers the child's resistance to a subsequent rheumatic infection. They are in any case precursors in point of time to the more obvious signs of rheumatic infection occurring in joints, nervous system, or heart, and quite apart from the discomforts and disabilities they entail in themselves are undoubtedly a source of lowered vitality in so far as they cause a deficiency of cutaneous excretion, interference with regulation of temperature, and reflex congestion of the splanchnic circulation. Under these circumstances it is obvious that such measures as are available should be taken to remove them. That cutaneous sensibility and vaso-motor responses to changes of temperature can be greatly improved by proper training no one will dispute. Apart from a suitable régime in other respects, a careful gradation of temperatures in immersion baths, together with douches, and friction to promote an active reaction, offer the best means of attaining this end. Whenever it is practicable a properly devised course of treatment at any well-appointed health resort will, as a preliminary to other measures, prove of the greatest benefit to these so-called "rheumatic" or rather "pre-rheumatic" children. So far as my own experience goes, it is an almost unknown thing for a child, other than an occasional case of Still's disease, for which hydrological treatment is of limited value, to be sent to a health resort for a course of treatment. Such luxuries are almost invariably reserved for their elders and betters. Yet I venture to think that we might often do more good to these children than to many of their crippled or rheumatic old relatives whom we are so often called upon to treat. When, as is no doubt very frequently the case, it is not practicable to send these juvenile patients to a health resort, a great deal can be done to train their cutaneous reactions by simple measures carried out in their own homes. As this training or hardening process must be continued over a long period of many months, a "course" at a watering place can, at the best, only be regarded as a preliminary measure. For their successful treatment, so far as hydrological measures are concerned, nothing is really required beyond the ordinary domestic bath, supplemented by some form of needle bath or shower. The exact gradations and alternation of temperature are matters to be determined for each individual case. The main principles to be observed are that the reductions of temperature should be gradual, that cold applications should not be sufficiently drastic to prevent a healthy reaction, and that the process of re-education should be continued for a sufficiently long time.

Turning to adults, we find that sluggishness of cutaneous vaso-motor responses and deficiency of sweat are largely responsible for the various types of "muscular rheumatism" and fibrositis. The tendency at the present day to label all forms of muscular rheumatism as fibrositis and regard all forms of fibrositis as due to infection would appear to be in some respects erroneous. Clinical evidence goes to support the view that a large proportion, at any rate of the less severe cases of "muscular rheumatism," are due either to accumulation of fatigue products, especially lactic acid in the muscles, or to autogenous toxins of gastro-intestinal origin. It is a matter of everyday experience that prolonged pain and stiffness of some severity may follow excessive exertion in those who are out of condition,

[1] *Proceedings*, 1925-6, xix (Sect. Baln., 1).

especially if they are no longer young. If the action of the muscles, or groups of muscles involved, though repeated often enough to cause fatigue, is not sufficiently strenuous to make the patient sweat, or, if he gets cold after exertion, the stiffness and pain are likely to be more severe.

It would appear as if the inadequate blood-supply to the muscles allows the accumulation of lactic acid, and possibly of other fatigue products, which act as an irritant either to the muscle fibres themselves, or to the strands of connective tissues which bind them together. It has been shown that when the amount of lactic acid present in the muscle reaches about 0·4%, a condition of complete fatigue results, in which the muscle fibres no longer contract, and that when it reaches 0·6%, a condition analogous of rigor mortis ensues. Furthermore, the production of lactic acid from the glycogen stored in the muscles is an anaerobic process, whereas its removal, largely due to reconversion into glycogen, is an oxidative process and dependent on a free supply of blood to the muscle. As the time goes on these attacks of muscular rheumatism, dependent upon exertion, tend to become more easily induced and more prolonged in duration. The repeated attacks of irritation, due to strain, and the accumulation of fatigue products have resulted in a definite organic fibrositis of the interstitial bands of connective tissue, and the patient becomes a "chronic rheumatic," for whom a "cure" is out of the question, and temporary relief the best that can be hoped for.

Much may be done by timely hydrological interference, to prevent this sequence of events. Relaxation of muscle by hot immersion baths, stimulation of blood-supply and cutaneous reactions by douches and massage, and a more free elimination of fatigue products and toxins by way of the kidneys and skin, remove the earlier symptoms of what may otherwise become a serious debility.

In the more widespread and serious type of fibrositis characterized by the deposition of nodules and sheets of what is virtually scar tissue in the fasciæ tendon sheaths, nerve sheaths, and so forth, the superficial vaso-motor reactions to variations of temperature are usually well marked. Patients with general fibrositis are extremely frigi-sensitive, suffering great discomfort from exposure to the slightest current of cold air. The more heavily they clothe themselves, the more their natural temperature reactions fall into abeyance and the more they seem to feel the cold. The diminished supply of blood to subcutaneous tissues and fasciæ impedes the rapid removal of toxins, or possibly of bacteria themselves, from these areas, and undoubtedly promotes the development of fibrositis. Though it may not be strictly correct to speak of treatment by baths, massage and so forth as being *preventive* in the face of a disease which is already established—yet provided that it is instituted early enough, this type of treatment may truly be said to be preventive—if carried out with vigour and repeated from time to time—of many of the most painful and crippling effects of the disorder.

It is, perhaps, in those conditions usually described as diseases of metabolism, such as obesity, gout, glycosuria and the metabolic disorders of the menopause, that hydrology offers the widest field in preventive medicine.

Obesity.—When we come to consider the preventive treatment of obesity we are at once confronted with the fact that various factors are usually at work to produce the condition. Any course of treatment likely to achieve an appreciable measure of success must take into consideration not only the matter of diet, but the question of endocrine balance and of chronic toxæmia. Just as a normal healthy condition of body and weight depends on a true balance between the energy-producing katabolic sympathetic on the one hand and the energy-conserving anabolic parasympathetic on the other, so any notable addition of fatty deposit depends ultimately on a want of balance between the two. While the association of obesity with pituitary or thyroid dystrophies is universally admitted, it is not so generally recognized that the ordinary type of general obesity is also largely

due to want of balance between the parasympathetic pancreas, on the one hand, and the sympathetic pituitary thyroid and adrenals on the other. The onset of obesity is not always to be explained in the terms of food and exercise. Many men and women tend to put on weight at middle age, not owing to any notable change of habits, because of any sudden access of gluttony or disinclination for exercise, but because for some reason or other, their sympathetic endocrines have become relatively inefficient. Among the causes of sympathetic exhaustion, chronic infection—intestinal or otherwise—must always be seriously considered. The fact that obesity frequently follows acute long-continued toxæmia, such as enteric fever, has long been recognized, and it is probable that in many other cases chronic infection, though often unsuspected, plays a more important part than is usually recognized.

Whatever treatment it is decided to adopt for the cure of obesity, everyone will agree that it should be commenced at the earliest possible moment. We all know how difficult it is to reduce the weight of a person who has been steadily putting on fat for years. The main indications, in addition to regulation of diet and removal of intestinal toxæmia by suitable waters or drugs, are firstly, to promote the katabolism of fat by hot immersion baths, vapour baths, or radiant heat, and secondly, to promote endocrine activity by the stimulating action of massage douches, needle baths, alternating spinal douches and so forth on the skin. As obesity is more often the expression of debility than of superabundant health, it is important to regulate the treatment in such a way that no further debility ensues.

Gout.—The treatment of gout by hydrology has always been regarded as one of the most successful features of this form of therapy. The object is not only to remove or mitigate the effects of previous attacks, but to prevent the occurrence of fresh ones, and in order to accomplish this we must have a clear conception of the primary underlying causes which we hope to remove. That gout is the result of disordered metabolism of nucleins whereby an undue proportion of purin bodies, instead of being excreted in the form of soluble urea, remains in the body as uric acid, and is eventually precipitated in the form of gouty deposits, everyone will agree. Also that the presence of uric acid in itself is not sufficient to cause gout. There must be some abnormal vulnerability of the joint structures, such as does not exist in other conditions, such as leukæmia, in which the uric acid content of the blood is enormously raised. What we have to do is to take the investigation a stage further back and inquire why certain patients develop this metabolic kink on the one hand, and undue vulnerability of joint cartilages on the other.

Now all clinical evidence goes to show a close connection between gout and gastro-intestinal disorders. The association of gout with habitual good living, lack of exercise, and portal congestion is too obvious to require elaboration, and frequency with which an attack is immediately preceded by symptoms of dyspepsia is equally well known. It is a mistake, however, to assume that the association of gout and the functions of digestion is necessarily and entirely a matter of the purin bodies in the diet. An attack of gout is not a matter of mathematics to be expressed in terms of a uric acid equation. Excess of sweets or starchy food is just as likely, if not more so, to precipitate an attack as an excess of meat. The true relation of gastro-intestinal disorder and gout lies in the occurrence of abnormal fermentations and intestinal toxæmia. It is rather as Professor Walker Hall puts it, "a condition of insufficient cellular resistance against the absorption of intestinal or autogenous poisons, leading to the formation of imperfectly formed metabolites." Once these abnormal fermentative actions, whether bacterial or otherwise, have become an established habit, attacks of gout will persist no matter how carefully you diet your patient. As Goodhart remarked, "Though you absolutely exclude all uric-acid forming food . . . you may wither up your patient into a shrivelled, juiceless prematurely-aged being, and there will yet, by some means or another, under

favourable conditions, be squeezed out of his tissues enough uric acid to form a large deposit of crystalline matter in his urine." The essential treatment in the prevention of gout must always be the removal of gastro-intestinal putrefaction. Drug treatment, in order to be successful, must be based on the same lines. As Luff remarks, "the classic remedies for gout have only two things in common; one that they relieve gout and the other that they check intestinal putrefaction, or diminish the absorption of its products or promote their elimination from the system."

These being the aims that we have or ought to have in view, it is obvious that the preventive treatment of gout offers a wide field for useful activity at many of our various health resorts. Removal of intestinal toxins, stimulation of digestion and relief of portal congestion by suitable waters, cautious stimulation of metabolic activity by warm immersion baths, hot douches and so forth, and the promotion of more efficient elimination by the skin and kidneys combine to form ideal methods of rectifying the antecedents of gout.

Glycosuria.—The claim that treatment by therapeutic baths or medicinal waters, or both combined, may have any appreciable effect in preventing glycosuria and diabetes, may at first sight appear somewhat extravagant. So long as we regard an organic destruction of the islands of Langerhans with consequent diminution in the secretion of natural insulin as the paramount cause of diabetes, it is obvious that no form of therapeutics other than diminution of carbohydrates on the one hand, and substitution of insulin from pigs or sheep on the other, is likely to be of any serious avail. We all recognize however that diabetes, even the so-called "true" diabetes, with hyperglycæmia and a typical sugar-tolerance curve, varies considerably in type, as between the young and the middle aged, and if we consider the circumstances which commonly lead up to what his doctor probably calls "a little gouty glycosuria," say in a middle-aged man, a condition which, if untreated, inevitably degenerates into a "true diabetes" we are led to think that in the earlier stages we are dealing with what is at any rate mainly a functional disorder rather than an organic disease. Professor Crile is, I think, responsible for the saying that "when stocks go down in Wall Street, diabetes goes up in New York," a saying which epitomizes many of the factors leading to the onset of glycosuria. The life of a business man with big interests and heavy responsibilities is apt to be fraught with varying emotions and excitements, leading to stimulation of the sympathetic, over-action of the suprarenal and excessive liberation of sugar from the glycogen stored in the liver and muscles. The exercise necessary to use up this sugar is not taken. Beyond an occasional or weekly round of golf his exercise is probably limited to pacing up and down the office carpet evolving plans for successful commerce. Pancreatic efficiency, on the other hand, leads to diminution. Abnormal sympathetic activity tends in itself to inhibit the action of the pancreas and the latter is further embarrassed by lack of exercise and portal congestion. Thus we have a purely functional disturbance of balance, excess of sugar liberated from the store on the one hand, and on the other a deficiency of natural insulin to deal with it. Such a condition is obviously one that lends itself to a course of hydrological treatment. Rest from agitation and excitements, and removal of portal congestion by salines, laxatives or other waters, and improvement in general circulation and muscular efficiency by baths, massage, and regular exercise, all combine to remove the various functional deficiencies involved.

The climacteric.—Though, in theory, the climateric must be regarded as a normal phase in the life of a woman and as such should entail nothing more than trivial and temporary inconvenience, it happens as a matter of fact that a large proportion of women at the "change of life" suffer very definite metabolic disorders. The complete readjustment of endocrine balance implied by the diminution and ultimate cessation of ovarian activity fails to take place. The normal close relationship between the ovary on the one hand, and the thyroid, pituitary and adrenals on the

other, no longer obtains, and in the absence of ovarian stimulus, these latter glands suffer a marked diminution of physiological activity with results with which we are all fairly familiar. Obesity, either of the general, or hypo-pituitary, or more often of the hypo-thyroidic type, is one of the commonest results, frequently accompanied by a somewhat characteristic type of villous arthritis affecting the knees and occasionally the wrists or other joints. The middle-aged woman of increasing weight, with a general thickening and loss of elasticity of subcutaneous tissues, due to widespread pannicular deposits, and complaining of painful, creaky, swollen knees, is sufficiently familiar to you all, and presents disabilities which, if allowed to go on, are going to impose a serious handicap to her for the rest of her life. I venture to think that there is no class of patient for whom treatment by balneological and allied methods is more likely to prove of benefit from the point of view of preventive medicine than the woman at the climacteric. A general diminution of metabolic activity with corresponding lowering of bodily temperature is a constant feature in these patients. Relatively hot immersion baths by which it is possible to raise the body temperature by anything up to four or six degrees Fahrenheit, from which it gradually falls to normal after two or more hours, forms a very valuable factor in treatment, especially when combined with massage, douches or such other measures as may seem to meet the case. Though endocrine therapy, especially thyroid, is of undoubted value in many of these cases, its value is greatly increased by combination with measures such as I have indicated above. Speaking of the sudden hot flushes and other disconcerting thermal phenomena so common at this period, Dr. Leonard Williams refers to the fact that "any kind of balneary measures, such as vapour baths, light baths, or hot packs, which succeed in raising the temperature to normal for an appreciable time, will afford more relief from these unpleasant symptoms than any drugs or hormones given by the mouth."

Hyperpiesis.—In spite of all that has been said and written about hyperpiesis or idiopathic high blood-pressure, so little is really known about its ætiology that it is not easy to formulate any principles of preventive treatment either by hydrological or any other means. The popular assumption that it is due to some form of auto-toxæmia has never been incontestably proved. The fact that intestinal toxins are all depressor, rather than pressor, in their action, appears to rule the digestive tract out of consideration, but is quite possible that in certain disordered forms of metabolism, pressor toxins may be elaborated elsewhere, and be responsible for the condition. The fact that hyperpiesis is associated with a shrivelling up of many of the more minute arterial twigs, and is, in a sense, compensatory in action, does not help us to understand the underlying cause. Though fatigue, strain, mental anxieties, and so forth, appear to be contributing factors, they can hardly be looked upon as the primary cause, and Lord Dawson's observation on a series of school girls suggests that the condition may exist from a very early age. The fact that early cases of hyperpiesis, without obvious organic changes in the vessel wall, respond to suitable hydrological treatment, suggests that the result may be due to detoxication, but there is one aspect of the question I should like to bring to your notice if only in a tentative fashion, and that is the factor of capillaries in determining the condition. All recent work on the capillaries goes to show that so far from being merely passive conductors of blood driven into them through the arterial tree, the capillaries are themselves capable of wide active variations of calibre. Under ordinary circumstances only a small proportion of capillaries is patent at any one time. Thus it has been shown that in a tetanized muscle the number of capillaries visible may be anything from forty to fifty times as many as when the muscle is at rest. Furthermore, in poisoning by histamine and in surgical shock resulting from extensive laceration of muscles, the paralysed capillaries may distend till they hold practically all the blood in the body. In view of all these facts I think it is not unreasonable to assume that the capillaries play a much more important rôle in determining the blood-pressure

than is usually recognized, and that their functional disuse and ultimate wasting may be primary ætiological factors. Also that the good results from hydrological treatment in the earlier stages are due to restoring the patency of capillaries more than to causing temporary dilatation of the smaller arteries and veins.

I am fully conscious that in these remarks I have only touched the fringe of what is a very wide subject. Many other conditions will, no doubt, occur to you, such as digestive disorders, functional derangements of the liver, and gall-stones, to mention only a few, in which hydrological treatment might be usefully employed in a preventive capacity. I have only mentioned certain diseases in which it might be so employed, to illustrate a generalization which I believe to be perfectly true, that medical hydrology might be much more widely employed as an agent of preventive medicine than it is at the present day.

Section of Electro-Therapeutics.

[*November* 21, 1930.]

Lupus Vulgaris treated by Quartz Light.—JUSTINA WILSON, F.R.C.P.Ed., D.M.R.E.Camb.

It is commonly held that of all forms of tuberculosis cutis, lupus vulgaris is the least affected by quartz light irradiation and that, failing heliotherapy, that ideal combination of heat and ultra-violet light, Finsen irradiation is necessary to obtain good results.

Finsen light treatment is, however, impossible in small, ill-ventilated, light departments. I have therefore brought up three cases to show that with a careful technique quite as good results can be achieved by quartz light alone.

G. M., aged 26, was placed under my care four years ago by Dr. Graham Little. An exceedingly bad case of lupus, with numerous foci on legs, chest and face. As to the nose, there was merely a flattened remnant of it left, the nostril and half the bridge were destroyed. She had been treated in the skin department for twelve years. The Wassermann reaction, tested repeatedly, had always been negative. The patient herself was anæmic, and was depressed on account of her sad deformity. This was a case where it seemed best to go carefully to try to restore the tone and vitality of the skin and arouse its own antituberculous defences rather than to aim at strong inflammatory reactions.

Technique.—General irradiations twice weekly from Jesionek lamps. Time, two to thirty minutes; distance, 100 to 60 cm. The local treatments were given with the patient lying down, each focus exposed in turn to the light of a Bach's alpine sun lamp. Time, two to ten minutes; distance, 50 to 20 cm. When the inflammatory reaction was at its height, from four to eight hours later, cold boracic compresses were applied by the patient at home to each treated area, (1) to prevent irritation, scratching and secondary infection, (2) to limit scab formation, (3) to put the hyperæmic tissues into a state of physiological rest. As the reactions died down, these alternate doses of inflammation and physiological rest were repeated again and again until, in 15 months, every ulcer had healed and the devitalized tissues had recovered their tone and elasticity. Also the patient's general health had vastly improved.

The loss of the nose, however, was a terrible drawback to her, preventing her from earning her living, and I felt that the time had come for a plastic operation, though Dr. Graham Little was pessimistic as to the probable result of grafting operations carried out on a lupus skin. Mr. Percival Cole thought it possible, and kindly admitted the patient to his ward in the Cancer Hospital, November, 1927.

After careful preparation (of nose, throat, teeth, etc.) the proposed addition was modelled by a sculptor. Guided by the plaster cast, portions of costal cartilage to stiffen nose-tip and margins of nostrils were embedded under the scalp, and the flap was outlined and turned down. Later on, the pedicle maintaining the blood supply was cut and trimmed, and she was discharged in October, 1928. Since then she has qualified as a shorthand typist.

Tuberculosis Cutis Verrucosa. — JUSTINA WILSON, F.R.C.P.Ed., D.M.R.E.Camb.

H. J. W., aged 34, brought to me June, 1927, by Dr. Martly of the Inoculation Department, St. Mary's Hospital, had extensive disseminated papulo-necrotic tuberculides on both forearms and elbows. On the dorsa of hands and fingers were numerous warts of papillomatory granuloma, with raised peripheral zones of board-like infiltration, with pigmentary change, separated by paler scaly plaques and incrusted patches.

History is of interest. At 4 years of age he had measles, followed by a series of abscesses on arms and legs, after which these successive crops of papulo-necrotic tuberculides began to appear. He was treated for these for years at the Hospital for Sick Children, Great Ormond Street, and was transferred at the age of 14 to the inoculation department of St. Mary's, where he had tuberculin injections.

Four years later, after an accident to his hand, tuberculous disease of the first metacarpal bone was set up, followed by a return of the original abscesses in the arm. These healed, leaving hands and arms in the condition in which I first saw them.

Treatment.—General irradiation with Jesionek quartz lamps twice weekly, with doses increasing from three to thirty minutes at a distance of 100 to 60 cm. to stimulate metabolism and general resistance; local irradiations—first, by Bach's alpine sun lamp, then by the more lumirous and penetrating light of a small open iron arc lamp, and later still by exposures to the Kromayer lamp, with compression at such intervals as to allow complete retrogression of each cellular reaction to light. Attendance has been intermittent as his business obliges him to be away a great deal. But there has been constant gradual improvement and disappearance of the crops of papulo-pustules and nodules, while the scaly incrusted plaques are replaced by new skin.

Lupus of Nose.—JUSTINA WILSON, F.R.C.P.Ed., D.M.R.E.Camb.

F. J., female, first came to Light Department, St. Mary's Hospital, January, 1930.

Condition on examination: Extensive destruction of both nostrils; some ulceration inside nose; cartilage not destroyed.

Treatment.—General light baths twice weekly and local treatment of each nostril by the quartz rod of a Kromayer lamp (1-4 minutes' exposures). Improvement has been steadily maintained.

Arthritis of Shoulder-joint, with Brachialgia. — JUSTINA WILSON, F.R.C.P.Ed., D.M.R.E.Camb.

M. Y., female, aged 61, referred to Light Department, St. Mary's Hospital, October, 1930, having acute pain in shoulder-joint and severe radiating pains down arms and into hands. Was first treated by constant current applied through shoulder-joint, followed by anodal arm baths. Little relief was obtained after five treatments, and therefore diathermy was substituted.

Method.—Fifteen minutes' transverse treatment to shoulder-joint, followed by fifteen minutes' longitudinal treatment to arm and hand, the peripheral electrode in this case being a shallow earthenware pan containing water in which the fingers rested. No diathermy pain was produced. There was marked relief after the first treatment and improvement since has steadily continued.

Discussion.—Dr. CURTIS WEBB said that, considering the lengthy period during which treatment by ultra-violet radiation had been in use since its institution by Finsen, it was somewhat remarkable that, in Dr. Wilson's first case, so long a time as twelve years should have been allowed to elapse before the patient came under that form of therapy. As he looked round the room at this—the first—clinical meeting of the Section, he thought it matter for comment that more members of the profession generally were not present to see

and hear what electro-therapeutics had been able to do. It was extraordinary how ignorant the mass of the profession were in this respect. Dr. Justina Wilson had proved the value of these methods. In her second case, also, he noticed that there was a thirty years' history of the condition, and that the patient was not referred for modern therapy until 1927. He hoped that these cases would be brought to the notice of those in other branches of the profession who might thus be induced to see that the work done in this department concerned themselves perhaps even more than it concerned those who were actually practising this speciality.

Dr. A. EIDINOW said that, in his personal experience, it was relatively easy to cure the tuberculous lesions of the skin by local treatment, but much more difficult to produce a beneficial effect on lesions of the mucous membrane of the nose. In one of his cases the skin had been cured in six months, but the result with regard to the mucous membrane was not yet satisfactory, even after two years' treatment.

Dr. JUSTINA WILSON in reply, said that in her third case (lupus of the nose) there had been great ulceration, but it was healing up very well under treatment with Kromayer applications. Treatment was begun in January 1930.

Old-standing Lupus Vulgaris: Results of Treatment by Fulguration —E. P. CUMBERBATCH, M.B.

Lupus nodules were first observed when patient was about 7 years old. He underwent various forms of treatment from time to time, including chemical caustics and X-rays. He is now 43.

When I first saw him the skin was scarred over the left shoulder and upper part of the arm. Numerous telangiectases were visible. A number of fresh nodules had appeared in the skin of the upper arm adjoining the scarred area, and it was for treatment of these new nodules that the patient had come to me.

On examination it was found that lupus nodules were still present in the scars that were originally treated.

I treated the fresh nodules by fulguration, using a diathermy machine and condenser couch. The first treatment was given four years ago. The applications were repeated weekly.

A number of smooth, soft scars are present on the outer part of the arm, in the regions formerly occupied by the nodules first treated by the fulguration.

I am now engaged in the treatment, by the same method, of the nodules in the scarred area. It is taking a much longer time than that occupied in the treatment of the nodules which had appeared more recently. At one time it seemed that no progress was being made, but when general ultra-violet ray treatment was given in addition, improvement was observed, and the disease is now disappearing, though slowly.

I should like to hear comments on this case. The few "virgin" cases I have treated, i.e., cases previously untreated by other methods, responded well to fulguration. Other cases were more obstinate and needed, in addition, general ultra-violet light treatment.

Discussion.—Mr. C. G. TEALL said that if Dr. Cumberbatch would subject this case to Finsen light treatment it would probably be cured. The number of cases of long-standing lupus which he (the speaker) had been able to cure entirely by X-rays and quartz light was very small. He had seen one case recently in which another radiologist had tried over a period of several years to cure a small patch of lupus on the face of a girl. This would improve until only one or two spots were left, and then the whole thing would recur. She was then treated at the London Hospital, with Finsen light, and now, after two years, she was completely cured, In many hospitals there were not the facilities nor the staff to carry out Finsen treatment, and such work as was done was carried out under great difficulties, but those who had been to Alton and seen Sir Henry Gauvain's results were convinced that if such cases could be put under ideal conditions and treated with Finsen light they would be cured.

Dr. G. B. BATTEN endorsed Mr. Teall's remark about Finsen light. He thought that the method used by Sir Henry Gauvain was not so tedious as that involved in the ordinary Finsen light treatment, and wonderful results were obtained by it.

Dr. CUMBERBATCH (in reply) said that Finsen light treatment was a lengthy procedure. It must be recognized that the electrothermic methods had not received a fair trial, and his own experience with regard to lupus was that in cases which had not been otherwise treated, those methods gave good results.

Cervicitis treated by Diathermy.—C. A. ROBINSON, M.B.

The skiagram shown is that of the pelvis of a woman who, two years ago, had a bone graft taken from the tibia and transplanted to fix the sacro-iliac joint, for the relief of severe backache. For over two years the patient had had leucorrhœa.

On examination, it was found that there was a well-marked cervicitis with erosion. It is quite common for the cellulitis accompanying cervicitis to cause backache, often spreading round the hips to the lower abdominal wall and to the front of the thighs below Poupart's ligament.

On digital examination one or both fornices may be tender, and on drawing the cervix forwards, pain in the back is produced or, as in this case, accentuated.

The radiogram shows very little, because the graft had been successful so far as the surgical operation was concerned. It had totally failed to cure the backache. The reason for producing the radiogram is only to introduce the subject of backache generally and its relationship to cervicitis.

In this case diathermy treatment caused rapid relief of pain and has resulted in the return of the cervix to normal appearances.

Dr. AGNES SAVILL said that at St. Bartholomew's Hospital also successful results had been obtained by diathermy in the treatment of cervicitis.

Three Cases of Subacute Dermato-myositis.—Sir ROBERT STANTON WOODS, M.D., M.R.C.P.

(I) A. B., female, aged 47, married. Two children younger, aged 8 years.

Onset, 1924, hands painful and swollen, pain spread to shoulders; 1925, feet painful and swollen; 1926 to 1927, condition at its worst. Treatment (previous to this date): Auto-vaccine (teeth), thyroid in large doses, sodium sulphocarbonate. Condition diagnosed as myxœdema, sclerodermia, Raynaud's disease.

September, 1927.—First examined. On that date could rise from her chair only with great difficulty and with assistance from her arms, Gait: A slow shuffle, and only possible by means of leaning on tables, etc.

All four limbs, as high as the elbows and knees, showed a hard, thick condition of skin, subcutaneous tissues and, as far as could be ascertained, muscles. Movements at toes, ankles, fingers and wrists showed extreme limitation. Malar eminence, neck and upper sternum, covered with similar tissue: extreme limitation of jaw movement; enlargement of the lymphatic glands behind the angle of each jaw. Considerable limitation of tongue movement. Teno-synovitis creaking at knees and ankles. Wassermann reaction negative.

Treatment.—Two courses of intravenous injections of arsenical preparations (these were extremely difficult to carry out). Many kinds of physical treatment.

Progress.—Great improvement in respect of gait and the use of the upper limbs. Physical signs practically unaltered.

(II) M S., aged 42, female, married, no children.

History.—Gradual onset from 1923 to 1925. Began with swelling and hardness of ankles. Upper limbs affected later.

First seen 1925. Skin of dorsa of hands, forearms and feet and front of legs, waxy and firm. Muscles of back of forearms and front of legs, hard and infiltrated. Scattered, pale brown patches on skin.

Considerable limitation of grip, especially right. Right wrist almost fixed; considerable limitation of movement at right elbow. Movement at knees slightly

limited. Area of corrugated skin over the inner aspect of the right upper-arm. Wassermann reaction positive. Skin sensibility normal. Temperature normal. Urine normal.

Treatment.—From March, 1925, to December, 1926, twenty-one intravenous doses of novarsenobillon with Hutchinson's pill simultaneously. Various courses of different kinds of physical treatment.

Progress.—Stationary, or slightly progressive, for two or three years. As late as 1928 thickening extended to skin over right trapezius. Finally, almost complete recovery.

(III) M. W., female aged 47, single, teacher. Onset, 1924 : legs and ankles swollen and painful. Early in 1925 : upper limbs also swollen and painful.

First seen, July, 1925. Then growing rapidly worse : hardening of skin and muscles of hands, forearms, feet and legs. Slight pitting of shins. Considerable limitation of grip, elbow extension, knee flexion and hip flexion. Shoulders slightly limited. Brown patches which disappeared and reappeared in various parts of the body. Wassermann reaction negative.

Treatment.—November and December, 1925, intravenous novarsenobillon, the last dose being followed by abdominal pain, vomiting and jaundice.

December, 1925, and January, 1926 : Four intravenous injections of sodium thiosulphate (0·6 grm.). Repeated courses of thyroid alternating with tincture of iodine in large doses.

Progress.—Steady improvement since 1925. Now without symptoms except some extensor fixation of the toes.

Mal-union of Radius. Treated by Diathermy.—L. D. BAILEY, M.C.

Motor-cycle accident, September 4, 1930.

Skiagram, September 5.—Showed fracture of middle of shaft of radius. Treatment by splints only, till September 25, then sent to Physiotherapy Department, St. George's Hospital. Practically no union present at this date. Treated by gentle massage on lower splint until October 7. Condition not markedly improved.

Skiagram, October 8.—Considerable overlap of fragments. Some visible callus. Diathermy treatment began October 9, and all other treatment was omitted from that date.

Four treatments given, as follows : October 10, 0·9 ampere for ten minutes, through site of fracture ; October 14, 1 ampere for fifteen minutes ; October 17, 1 ampere for twenty minutes ; October 21, 1 ampere for twenty minutes.

Skiagram, October 23.—Considerably more callus. Two more diathermy treatments were given, after which the course was discontinued as, clinically, the bone seemed to be firmly united.

Discussion.—Dr. PIERRET (France) said that lack of callus was very often only due to the fact that the nourishment of the two ends of the bone was not sufficient. Extensive work had been done in similar cases ; perhaps in Dr. Bailey's case the diathermy had had a special action on the nourishment of the two ends of the radius. In France, diathermy was employed in these cases, but they were also treated by hot-water baths and compresses, and the two methods of physiotherapy, diathermy on the one hand, and simple heating on the other, probably acted in the same way, namely, by causing vaso-dilatation of the arterial capillaries and better nourishment of the tissues.

Dr. C. B. HEALD said he agreed with what Dr. Pierret had said about the necessity of increasing the nutrition of the part. The difference between delayed union, mal-union, and non-union had to be recognized. The first stage was to improve the nutritional condition, and in these cases he always began with the direct current, using the positive pole, and the arm in the bath, on the ground that the direct current promoted the flow of lymph from positive to negative. When that was not effective, diathermy, for increasing the blood-supply

to the part, was absolutely essential. It was necessary to counter-irritate the tissues, and for that purpose he used a strong localized cathode current. He was now speaking of the stage when the nutrition of the part had been improved. During the years that Dr. Howitt, his colleague, and himself had been at the Royal Free Hospital, treating these cases by increasing nutrition, increasing blood-supply, counter-irritation, and increasing the lime salts by ultra-violet light, they had not had one single case of non-union of bone.

Dr. A. E. BARCLAY said that some years ago he had used a sinusoidal wave current with great benefit, especially in the treatment of un-united fractures. By the use of special splints in which he incorporated electrodes, the muscles were kept healthy by the daily—or even more frequent—application of electric stimulation, without disturbing the position by removing the splint (*Arch. of Rad. and Electrology*, Dec., 1918, xxiii, 205). Another point that arose out of this method was that there appeared to be an almost entire absence of adhesions in the immobilized joints if the muscles were stimulated two or three times a day. On several occasions he had kept joints at rest for six or eight weeks and had found an entire absence of adhesions at the end of that period, the limitation of movement being solely due to the shortening of the muscles, which rapidly regained their normal length when brought into full use.

Dr. CEDRIC HILLIARD said that surgeons ought not to delay in recommending these cases for physiotherapy. He noticed that in the case Dr. Bailey had shown, three weeks elapsed before he (Dr. Bailey) was asked to do his best with the case, and it was rather unfair that he should be asked to clear up a condition in large part due to neglect. Everyone would agree that much better results were obtained if an early and fair chance were given to the physiotherapist.

Dr. C. A. ROBINSON said that at his hospital a large number of non-united fractures were treated by electrical methods. When he began his work, he was familiar with Dr. Barclay's treatment of non-united fractures by the sinusoidal current, but he thought that he himself would try the direct current, and this was fairly successful. He had had a case, however, in which a plate had been used, and he was accused of having loosened the plate by the application of the current. Whether that had really occurred or not he would very much like to know. But since that incident, he had always used the sinusoidal current, and no case of un-united fracture had failed to heal.

Dr. FLORENCE STONEY mentioned a case of osteomalacia in which the patient had six pelvic fractures. She had been treated by diathermy for nine months without any success. The treatment was then changed to ultra-violet light, and twelve months afterwards the patient, who had previously had to be carried, was able to walk to the hospital for further treatments. When she (Dr. Stoney) last saw her, she was engaged in scrubbing floors. That was a case of cure by ultra-violet light rather than by diathermy.

Dr. E. P. CUMBERBATCH said that Dr. Bordier, of Lyons, had done excellent work in the treatment of poliomyelitis by diathermy. In his own experience, children with this condition had been placed in hot baths, in addition to having the sinusoidal current applied. This current produced reflex effects, and by putting the patient in the bath and giving the sinusoidal current, rather a deeper vaso-dilatation was secured.

Dr. CURTIS WEBB said he would suggest that a combined meeting might be arranged between this Section and the Sections of Surgery and Orthopædics, in order to decide whether some form of physiotherapy should be automatically applied in almost all cases of fracture. No surgeon could tell at the outset whether he was going to get perfect union, delayed union, or non-union. Mal-union possibly constituted a different question, but if physiotherapy was to be of maximum value in the treatment of fractures, there ought to be a definite consensus of opinion on the point and an *ex cathedra* utterance laid down that physiotherapy should or should not be used in the majority of cases of fracture.

Dr. G. B. BATTEN agreed with Dr. Curtis Webb. He had recently treated several cases of fracture of the hip-joint. He had had the aid of orthopœdic surgeons, and had been rather aghast at the length of time it had taken to get the leg well after the hip itself had recovered. A discussion on the value of physiotherapeutic methods in a combined meeting might be of assistance on all sides.

Intra-pelvic Protrusion of Acetabula.—E. J. DECK, L.R.C.P., M.R.C.S.

Mrs. M., aged 55, came to the London Clinic on the advice of her doctor for treatment for arthritis, April, 1930.

Two years ago had begun to notice increasing stiffness and loss of movement in both legs; was easily fatigued.

On examination: Abduction of legs impossible. Other movements slightly impaired; this latter condition was, she said, a recent disability, whereas she had first discovered the difficulty of abduction on getting married about eighteen years previously. Finding the marital act in the natural way impossible, she consulted her mother, who informed her that she had had the same disability all her life. It is regrettable that skiagrams of the grandmother's pelvis are not available or obtainable, but there can be no doubt that the peculiar condition shown in the skiagram of the pelves of both mother and daughter to-night has passed through three generations, which is strong proof that it is congenital.

From other history obtained, an examination of the cervix was made and showed the presence of a small erosion and a small polypus, and it was thought that the rheumatic pains of which the patient complained were due to this seat of infection. Treatment by intra-pelvic diathermy was applied, and the patient has been greatly relieved.

Seen November 5, 1930. No return of the rheumatism; very well in health.

Paget's Disease.—E. J. DECK, L.R.C.P., M.R.C.S.

Mr. T., aged 63. The skiagrams demonstrate a case of Paget's disease, the only point of interest being the typical diagnostic patch in the skull.

Discussion.—Dr. KERR RUSSELL said that in 1925-26 his wife and himself had treated three cases of Paget's disease by ultra-violet radiation. Definite improvement had resulted after a comparatively short course of treatment, especially in the tibiæ. Ultra-violet irradiation was a sound treatment for rickets, osteomalacia, chronic osteomyelitis, and delayed union of fractures, owing to its definite action on calcium and phosphorus metabolism.

Dr. DECK (in reply) said that he had treated one of his cases with ultra-violet light, but he had not obtained a skiagram of the condition afterwards, and could not say whether ultra-violet light had improved the condition or not.

Double Rudimentary Cervical Rib.—C. B. HEALD, C.B.E., M.D.

Patient, female, aged 46.

History.—Pains down both arms, with definite weakness of interossei, when seen by Mr. Norbury in August, 1930. Pains had been persistent for eighteen months and were growing worse and extending down shoulders.

3.9.30.—Double metronome Bristow to both trapezius muscles. Rapid improvement as trapezius muscles came into tone.

Rationale of Treatment.—If trapezius muscles could be increased in tone, shoulders would be lifted and drag taken off brachial plexus. This case is one of several treated successfully on similar principles. Is it reasonable to expect this result as a rule, and to advocate this method as a routine treatment to be tried before operation?

Discussion.—Dr. CURTIS WEBB said that he had had an extremely similar case about two and a half years ago. He had tried diathermy, sinusoidal current, and galvanism, to the best of his ability, and had to confess that after treating it he had failed to get any result whatsoever. The case was subsequently sent to Sir Percy Sargent, who operated, and the operation was attended with absolutely satisfactory results. He was afraid that definite pressure on the brachial plexus, either by bony or cartilaginous formation, could not be removed by physiotherapy, great as were its merits, and under these particular circumstances surgical operation became a necessity.

Dr. L. D. BAILEY said that the pain due to cervical rib often appeared as the patients grew elderly, and was probably due to a dropping of the shoulder from loss of tone of the muscles. He could quite realize that improvement of the tone of the trapezius muscles by stimulation with the Faradic current would temporarily benefit the condition, if not permanently cure it.

Dr. HEALD (in reply) said that he did not quite agree with Mr. Curtis Webb. His own aim in suggesting physiotherapy had been not to obstruct the surgeon, but simply to give these cases a preliminary trial in this manner, rather than to consider surgical operation in the first instance.

Clinical Section.

[*November* 14, 1930, *continued.*]

Aortic Aneurysm and ? Syphilis of the Lung.—F. E. SAXBY WILLIS, M.D.

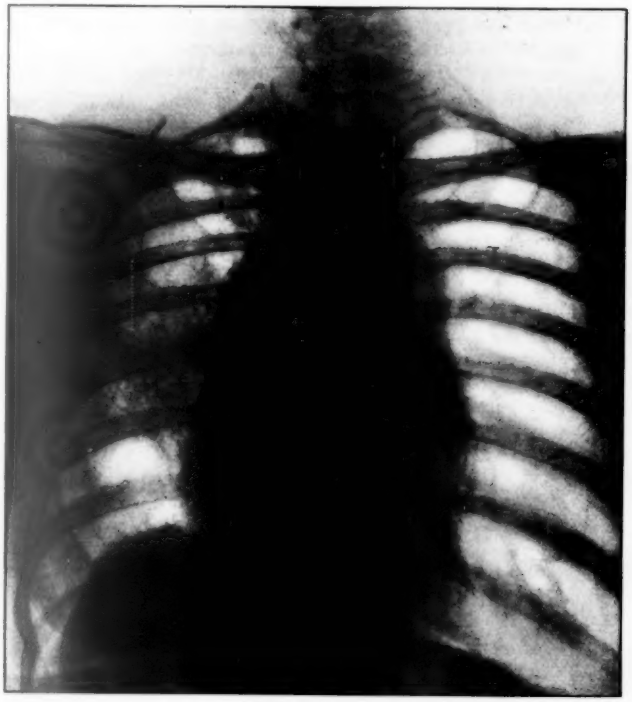
L. L., female, aged 53.

History.—Cough and expectoration of frothy sputum with dyspnœa, palpitation, and pain in the left side of the chest, worse on exertion. Symptoms were first noticed after an attack of acute bronchitis in January, 1930.

Past History.—Subject to bronchitis for sixteen years. Appendicectomy in 1924. Nephropexy in 1928.

Family History.—Three stillborn children.

On Examination.—Patch of ulcerative dermatitis on right side of forehead.



Dr. Saxby Willis's case of aortic aneurysm.

Heart: Apex beat in fifth space, 2 in. to left of sternal border. Area of cardiac dullness increased transversely at level of second intercostal space. The aortic second sound is accentuated.

Lungs: Impaired resonance and bronchial breathing over right upper lobe. Movement of upper right side of chest restricted.

Skiagram shows a diffuse aneurysm of the arch of the aorta, appearances suggest dissecting aneurysm of descending portion of arch. Heart drawn to right. Lung fields show a diffuse interstitial fibrosis of upper and middle zones of right lung. Diaphragm drawn up on right side by adhesions. (See fig.)

Wassermann reaction + +. Sputum negative for tubercle bacilli.

Treatment.—Potassium iodide gr. v-xv t.d.s. for six weeks; four intramuscular injections of calomel gr. 1½; four injections of sulfarsenol 0·5 grm. (This was not well tolerated.) One injection of intramuscular bismuth 0·1 grm.

I think this is a case of true syphilis of the lung. The lung is contracted, as shown by the fact that the heart is pulled over to the right; the diaphragm is pulled upwards by fibrous strands, and there is, more particularly towards the centre and upper part of the lung, a very definite dullness on percussion and loud bronchial breathing in front, and occasionally there have been moist sounds, which have cleared up since antisyphilitic treatment was begun. The type of fibrosis present is a peculiar one. In one or two places are small circular areas, less opaque towards their centre; these may be gummata, which have partly broken down in the centre. Around them are strands of peribronchial fibrosis.

The lung condition has improved somewhat since treatment; cough and dyspnœa are less, and what sputum there was has now disappeared.

Should I go on with the arsenical treatment, knowing that the patient has reacted unfavourably to it?

Discussion.—Dr. E. STOLKIND said he agreed with giving, in such a case as this, a combination of treatment: iodide, mercury and salvarsan, but in only small doses, the course being repeated every four or five months. Of 132 cases which he (the speaker) had reported of syphilitic disease there were sixty-one of aneurysm, but in none of the post-mortem examinations had syphilis of the lung been found.

Dr. SAXBY WILLIS (in reply) said he was much interested in Dr. Stolkind's figures. He would try minimal doses of arsenic, and note the result.

Thrombo-angiitis Obliterans.—ST. J. D. BUXTON, F.R.C.S.

H. E., male, aged 49, formerly a motor engineer.

Shown at a meeting of the Section in 1923,[1] when it was pointed out that he was not a Jew. Symptoms began in the legs in 1921. In November, 1922, sympathectomy was performed on the right femoral artery. The right leg was amputated shortly afterwards. In August, 1925, the left leg was amputated. In December, 1925, it was noticed that the right radial artery was smaller in volume than the left. In 1929 the right radial artery showed no pulsation. In 1930 pain became severe in the fingers of the right hand. At times the fingers of this hand were blue. In October, 1930, a patch of gangrene appeared on the end of the middle finger. The patient is not a heavy cigarette smoker; for eight years he has hardly smoked. Wassermann reaction negative.

A microscopic section of the vessels of the right leg showed an obliterative endarteritis.

Discussion.—Dr. PARKES WEBER recommended a trial of angioxyl, the insulin-free pancreatic extract, which had been used a good deal in France, after insulin for such cases had been given up. Angioxyl seemed to be specially serviceable in removing the pain in some cases. A similar German preparation was Kallikrein.

The PRESIDENT asked whether angioxyl was a specific, or a method of giving protein shock. He gathered that one was not likely to get much more improvement from this substance than from the intravenous use of typhoid vaccine, and so he assumed that it was in the nature of protein shock. It raised the temperature and increased the pulse-rate.

Dr. STOLKIND said that in cases of angina pectoris the effect of angioxyl was similar to that of protein therapy. He had tried yatren casein, with satisfactory results. Gradually increasing doses were used.

Dr. PARKES WEBER (in reply to the President) said he did not think that the preparation mentioned acted merely by non-specific protein shock. He suggested that in future it might be tried before resorting to such operations as peri-arterial sympathectomy in cases of chronic arterial ischæmic disturbance in limbs.

[1] *Proceedings*, 1923, xvi (Clin. Sect. 14).

Fracture-dislocation of the Ankle-joint, Reduced by Operation Three Months Later.—PAUL BERNARD ROTH, F.R.C.S.

Frederick R. C., aged 37, was first seen on July 4, 1930, stating that eleven weeks previously he had fractured his right ankle and had it set at a provincial hospital.

The limb was in plaster, and the skiagram, taken for Dr. Remington who sent the patient to me, showed that there was a "type III" fracture of the lower end of the tibia. A portion of bone, including the posterior half of the articular surface, had been broken off and displaced upwards, allowing the astragalus, with the whole foot, to dislocate backwards.

Operation was performed under a tourniquet five days later: the joint was opened on the outer side and the foot turned inwards out of the way, exposing the broken lower articular surface of the tibia. The posterior half, which had been broken off and displaced upwards, was freed, brought down into proper relationship with the main portion of the tibia, and fixed there with a steel screw. The astragalus, and with it the rest of the foot, was replaced beneath the re-formed tibia, and the wound was closed, plaster being applied.

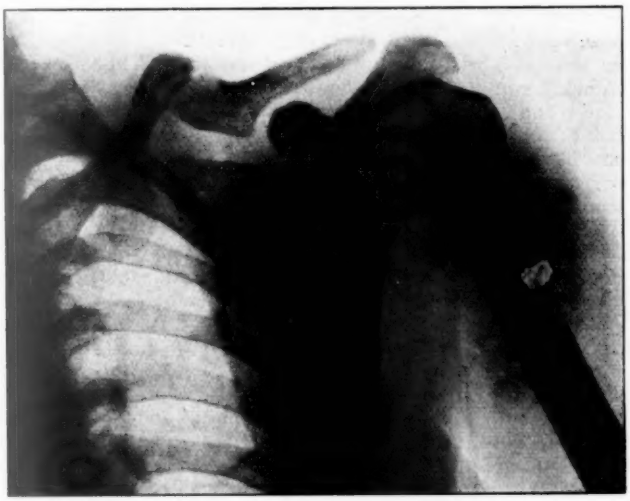
The skiagram, taken four days later, shows perfect replacement of fracture and reduction of dislocation.

There was an uneventful recovery, and when seen October 16, 1930, three and a half months after operation, there was very good movement at the ankle-joint, and the patient was able to walk for miles without discomfort.

Multiple Osseous Defects.—HAROLD AVERY, M.R.C.P.

A. G., female, aged 32, single, was first seen on account of backache, due to fibrositis.

She has a repaired hare-lip and the speech is typical of a cleft palate. The latter has been repaired in early infancy, but the result is not good; the small, sclerosed, immobile soft palate cannot close off the naso-pharynx and hence the speech defect. The middle of the right clavicle is prominent and projects forwards. There is a certain amount of mobility at this point. The forearms are fixed in a



Skiagram of right shoulder (Dr. Avery's case).

semi-prone position, there being no power of either pronation or supination. As a result of this incapacity she is unable to hold a spoon properly, but must hold it in baby fashion in order to bring it to the mouth. The cranium is normal and no other developmental defect is present.

X-ray examination shows a right cranio-cleido dysostosis; the portions of the clavicle formed from the two primary ossification centres are both present, but are not united. The outer segment looks like a normal outer half placed the wrong way round. There appears to be a definite joint between the two portions. Bilateral radio-ulnar synostosis is present, the upper ends of, the radius and ulna being ankylosed. There is no definite radial head, the two bones being merely fused together in one mass. The lower ends of these bones are normal on both sides. A skiagram of the lumbar-sacral region reveals no abnormality which might account for the backache complained of.

As far as the patient is aware, there is no other developmental defect in the family.

Dr. PARKES WEBER remarked that in the present case the cranio-cleido-dysostosis was very incomplete; in fact, it was limited to one clavicle, though associated with various other congenital-developmental abnormalities.

Branchial Cyst.—ERIC A. CROOK, M.Ch.

D. T., boy, aged 3½, has a swelling in the left side of the neck, behind the angle of the jaw. This swelling has been present since birth and has been noticed to vary in size from time to time.

It is in the position of the second branchial cleft, and it seems to move with the pharynx, and has a soft, semi-elastic feel. It does not show any signs of inflammation. I think it should not be operated on.

Mr. JAMES CARVER said he thought that this swelling was a nævolipoma. He had never seen a branchial cyst in a child under 15 years old; they usually manifested themselves between the ages of 15 and 25. This swelling was superficial to the deep fascia, had a bluish appearance, and became smaller on compression.

Hodgkin's Disease.—C. WORSTER-DROUGHT, M.D., and T. R. HILL, M.D.

H. P., male, aged 28, first seen July, 1929, complaining of a firm, hemispherical swelling over the manubrium sterni for two months. This had been gradually enlarging. A small swelling had been present in left side of neck for more than two years. On admission: several hard glands detected in left supraclavicular region. No enlargement of the spleen and, apart from sternal swelling and enlarged cervical glands, patient showed nothing abnormal.

Previous History.—Tuberculous glands removed from right side of neck in childhood (scar present).

Progress.—Bioscopy of gland removed from left side of neck showed "lymphoid tissue largely replaced by fibrous tissue. Eosinophil cells present in fair numbers. Occasional doubtful giant-cell. Section suggests lymph-adenoma but is not typical." Tissue from the sternal swelling showed chronic inflammation only. *Blood-count*, July 29, 1929: Hb. 74%; R.C.'s, 4,600,000; C.I., 0·8; no abnormal red-cells. W.C.'s: 22,100 per c.mm.; polys., 76%; lymphos., 16%; large monos., 5%; eos. 3%. Wassermann reaction, negative.

X-Ray examination of sternum, July 12, 1929: "Sternum appears unaffected." In August, 1929, the patient developed diphtheria and for some months after recovery from this condition he remained a "carrier."

Readmitted to hospital April, 1930. Sternal swelling much larger; was then 3 in. in diameter, not attached to skin but immovable over sternum. Enlarged glands in left axilla. Lungs, heart and circulation, abdomen, and nervous system

normal. Blood-pressure 155/75. Spleen not palpable; urine normal. No glands palpable in right axilla or in inguinal regions. An X-ray examination of sternum on May 1, 1930, showed "numerous enlargements in posterior mediastinum. Manubrium sterni shows great bone destruction and also irregular proliferation of new bone." Blood-count, May 13, 1930: Hb., 50%; R.C.'s, 3,800,000; C.I., 0·65; no abnormal red cells. W.C.'s: 47,000 per c.mm.; polys., 84%; lymphos. 8%; large monos., 5%; eos., 3%.

Present condition.—Mass extending from sternal end of left clavicle above to fifth rib below; laterally from just to right of sternum to within one and a half inches of left anterior axillary fold. Two more recent portions of swelling show softening and superficial reddening. Impaired resonance with diminished breath-sounds over right side of chest posteriorly, from just below spine of scapula downwards. Enlarged glands on both sides of neck, in both axillæ, and, to a slighter extent, in inguinal regions. X-ray examination, October 24, 1930: "Shifting dullness in right side of chest through which a mass can be seen projecting from mediastinum to the right. Other smaller masses project to left." Spleen and liver edge impalpable.

Blood-count, October 30, 1930: Hb., 60%; R.C.'s, 4,150,000; C.I., 0·72; no abnormal red cells. W.C.'s, 22,000; polys., 86%; lymphos., 7%; large monos., 3%; eos. 4%.

Commentary.—When first seen this patient presented some difficulty in diagnosis. He showed only the sternal swelling and one palpable gland in the neck. Microscopical sections of the swelling only revealed signs of chronic inflammation. The gland was suggestive, but not conclusive, of Hodgkin's disease, showing no definite giant cells. The diagnosis was also complicated by the fact that tuberculous glands had been removed from the neck in childhood. The patient was treated with arsenic and deep X-ray applications; the latter appear to have produced softening in the sternal swelling, but the general condition has steadily deteriorated. Further groups of glands became enlarged and the diagnosis of Hodgkin's disease became more certain, being eventually proved by the microscopical examination of a further gland which showed typical lympho-adenomatous changes.

It was difficult to decide the site of origin of the sternal tumour. From the diffuse absorption of the manubrium as shown radiographically it was considered that the growth probably originated in the reticulo-endothelium of the sternal bone-marrow.

Generalized Osteo-chondritis.—By A. DICKSON WRIGHT, M.S., F.R.C.S.

J. P., boy, aged 9 years 11 months. During the second year of his life he had been treated for "rickets" by complete immobilization on a board. He received further treatment at the age of 7, and by a famous bone-setter at the age of 8. The family history was entirely normal. The boy is an only child. He never suffered pain and the treatment was always for the deformity which is seen in fig. 1. There is a lordosis of the lumbar region with a dorsal and cervical kyphosis, so that the head projects forward. The hips and knees are always flexed because there is a shortage of extension of 70° approximately in each hip-joint. The boy walks and runs well but in a crouching position as if chasing his centre of gravity. If the head is pushed back the knees have to be flexed still further because the spine is "poker" rigid and the hips are incapable of further extension.

Skiagrams reveal abnormalities in practically every epiphysis of the body, and changes in other ossifying centres characteristic of the disease known variously as osteochondritis or osteochondropathy. The term dyschondroplasia or chondrodysplasia is sometimes applied to this disease, although used by Ollier to describe a different condition.

The following sites show the disease most distinctly (figs. 2 to 6): (1) Patellæ (Larssen-Johansson disease); (2) tarsal scaphoid (Köhler's disease); (3) carpal

semilunar (Kienboch's disease); (4) epiphysis of os calcis (Sever's disease); (5) the astragalus on both sides; (6) the vertebral bodies are all flattened (Calvé's disease), producing the condition of generalized platyspondylitis described by Lance and Cornell; (7) the metacarpals of the index finger and thumb on both hands show infraction of the end of the bones opposite the epiphyseal ends giving the appearance of an epiphysis at both ends; (8) the pelvis shows changes in the acetabula, the pubic

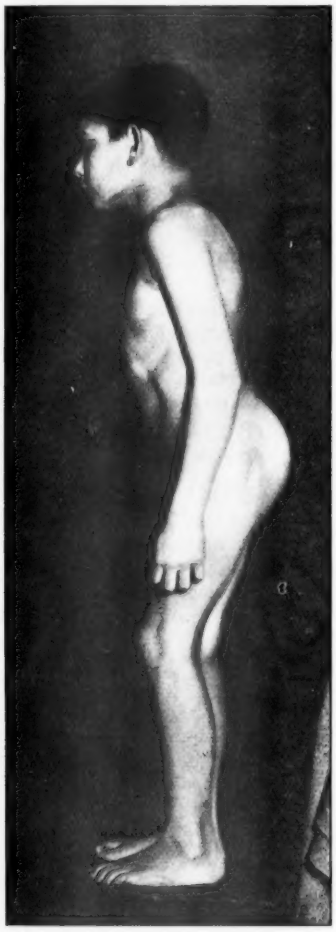


FIG. 1.—Shows characteristic posture and disproportion of length of arms to trunk.

symphysis and at the ischio-pubic junction on both sides; (9) the upper ends of the femora show changes in the heads (Calvé-Legg-Perthe disease), and the great and small trochanters. The lower ends of the femora show irregularity of the joint surface (? König's disease), with commencing separation of a loose body on the right side.

The disease has been separately described in thirty-six different situations; some

FIG. 2.—Köhler's disease, Sever's disease, Stern's disease, of lower end of tibia, and changes in astragalus on both sides.

FIG. 3.—Shows changes in femoral heads and both trochanters, pubic bones, and acetabula.

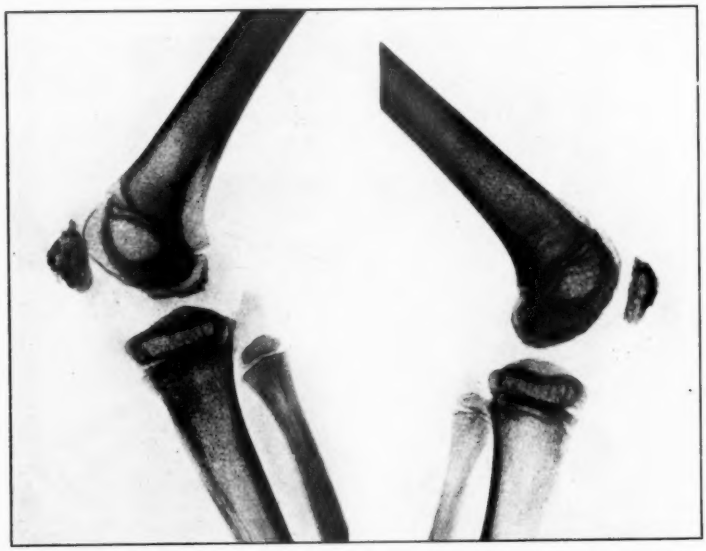


FIG. 4.—Patellæ showing Larssen-Johansson disease and König's disease of femoral epiphysis.

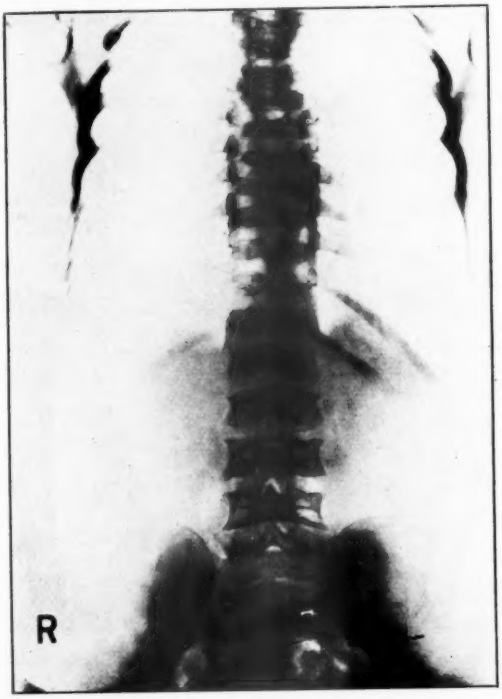


FIG. 5.—Generalized platyspondylitis.

of the epiphyses commonly affected have not yet appeared in this boy, but apart from these he seems to have the disease in every possible site.

Mentally, he is more than usually acute.

The generalization of the complaint in this case rather tends to disprove the traumatic and embolic theories of ætiology. Mau has produced what he considers to be this disease in the caudal vertebræ of rats by the simple manœuvre of stitching the tail underneath the abdominal skin. A case of this type is most easily explained by an endocrine factor; there must be some hormonic control of the complex ossifying processes in the child. It is noteworthy that in this case the pituitary fossa is unusually small. The disease in the hips has been repeatedly reported with

FIG. 6.—Changes in radial and ulnar epiphyses, carpal and metacarpal bones, and phalanges.

Fröhlich's syndrome and explained by the extra strain produced by the adiposity characteristic of this complaint.

The prognosis in this case is unfavourable as regards spinal deformity. There is bound to be a certain amount of dwarfism, and already the arms can be seen to be out of proportion to the stature (fig. 1). Secondary arthritis may develop from the abnormal posture. When fresh epiphyseal centres appear (e.g., vertebral epiphyses), the disease will appear in these centres also.

I consider that the most valuable treatment would be a double osteotomy of the femora to overcome the flexion deformity. It is quite possible that if the boy is able to stand erect, the spasticity of the back muscles will disappear and the spine acquire a certain degree of movement.

Further Report on a Case illustrating the Banti Syndrome in Syphilis. (*Shown at a Meeting of the Section on May 10, 1929*[1]).—HUGH S. STANNUS, M.D.

The two points in favour of the case being one of syphilis were the nodular liver on palpation, and the positive Wassermann reaction. The patient, a woman aged 47, left the French Hospital of her own accord, was readmitted on July 7, 1930, after

1 See *Proceedings*, 1929, xxii, 1228 (Clin. Sect. 74).

another severe bleeding into the stomach, and died three weeks later after a further hæmorrhage.

Post-mortem examination.—Well nourished woman with considerable deposit of subcutaneous fat. Right lung almost completely adherent to chest wall; left lung showed many dense adhesions at base. Heart and large vessels small, but exhibited no obvious lesion except small area of slight puckering in first part of arch of the aorta. Kidneys of normal size and apparently otherwise normal.

Marked ascites present. Liver weighed 1,500 grm., and showed marked multilobular cirrhosis with fatty changes; grossly deformed and adherent, by a thickened capsule, to the diaphragm and adjacent organs. The spleen weighed 830 grm., was of firm consistence and exhibited marked perisplenitis. No other pathological lesions were discovered except some small fibroids in the uterine wall and a mucocele of the fimbriated extremity of the right Fallopian tube.

There is a recent paper on this subject, with full references, by H. M. Korms (*Amer. Journ. Med. Sci.*, 1930, clxxix, 811). The post-mortem findings in the case reported closely resemble those mentioned.

Section of Epidemiology and State Medicine.

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Food as a Preventive of Disease.

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WELL-BEING is dependent upon two factors, heredity and environment, and the most important environmental influence to which we are subjected is food. Food is an absolute necessity for life; it enters more closely and intimately into the metabolic processes and affects them more profoundly than any other external influence. Though even food cannot create a metabolic quality which is lacking, it may be capable to some extent of counteracting or compensating for hereditary deficiency, and it certainly supplies the materials which a good constitution can turn to the best account in metabolism and without which even the best constitutional make-up would be powerless to resist "the thousand natural shocks that flesh is heir to."

The body, when properly fed and well nourished, has extraordinary powers of resistance to disease and adverse circumstances. Breast-fed infants of well-nourished mothers can withstand conditions of life that would be fatal to others not so well fed. The children of crofters, though often living in overcrowded hovels, are remarkably free from rickets, whereas children living in better surroundings but improperly fed fall readier victims to this disorder of nutrition. The incidence of tuberculosis in a community appears to be closely correlated with the food supply; it diminishes when the food supply is ample and increases when for one reason or another food is difficult to obtain and the quantity and quality of the diet become inadequate. Troops can withstand great hardships if their rations are ample and suited to their needs, and the ravages of infectious diseases, such as typhus, are especially severe amongst those whose resistance has been impaired by lack of proper food. During the middle ages the relationship between "famine and pestilence" was well understood and the phrase had terrible significance.

It is by no means a simple matter to say with certainty what is sufficient and suitable food, or when a diet may be regarded as completely satisfactory. Some animals, such as the larvæ of certain butterflies, will eat only one specific kind of leaf, and in such cases it is easy to say what is a proper and suitable diet. Man, however, would seem always to have eaten everything of an edible nature which happened to be available. In other words, his diet seems to have been as varied as his circumstances permitted. In this he appears to have been right; recent research has shown that the keynote of a successful diet is variety. It is only by variety of the right kind that the body can obtain all the various constituents which are essential for normal nutrition. No single food-stuff will meet satisfactorily the needs of the adult. The maize grain, though an admirable food material for the young maize plant, is an imperfect and inadequate food for man and would have to be supplemented in other directions if health, or even life itself, is to be maintained. On the other hand, milk, one of the few foods expressly manufactured by an animal

for an animal, is a perfect food for the young; indeed, it is the only food available, and its constitution is such that even for the adult, milk and milk products form some of the most valuable foods obtainable.

The view is generally current that primitive man was in some way more favourably situated in regard to his diet and nutrition than man of the present day, but I do not think that this view rests on strong ground. Primitive man had to be content with whatever food was available, and this must often have been scanty, difficult to obtain, and not always suitable dietetically. In this country, even so recently as a few hundred years ago, food resources were limited; harvests failed periodically, famine ensued, and was usually accompanied or followed by outbreaks of disease. To-day, however, the world is our larder. From both northern and southern hemispheres, with their alternating seasons, comes a constant and uniform supply of food in great variety, much of which is produced under more favourable natural conditions than exist in this country. Never in our history have we been better supplied with food from which satisfactory diets can be constructed. Yet in spite of this, a considerable proportion of our population is living on diets which cannot be regarded as ideal from the nutritive standpoint. This may be due in part to ignorance and to established habits and tastes, both of which are not insuperable, and in part to apathy, which is not so easily remedied. But amongst a large section of the population, price is perforce an important factor in determining the composition of a diet. Cereals (flour, bread) are relatively cheap and abundant, and consequently tend to bulk largely in the diet, whilst the more expensive, dietetically valuable foods—milk and green vegetables—are frequently lacking. Ill-balanced diets of this sort are, unfortunately, not uncommon.

Present knowledge permits a good deal more to be said about diet than that an inadequate diet conduces to mal-development and lack of resistance to disease. It is possible to indicate specific disturbances to metabolism, with resulting abnormal development and lack of resistance to disease, which derive in many instances from specific defects or errors in diet.

Thus a characteristic form of ophthalmia has now been shown to be due to a deficiency of vitamin A in the diet. It has occurred on numerous occasions in recent years in Denmark, Newfoundland, and Labrador, and lately cases have been reported in the Johns Hopkins Hospital, Baltimore. In parts of Austria and Roumania during the late war when food was limited to maizemeal and soup made from bran and vegetables, and in Denmark, when the diet was limited to skim milk, oatmeal and barley soup, this disease made its appearance, especially in children. The administration of butter, cream or cod-liver oil, or even the consumption of fish in liberal amounts, promptly relieves the condition. In 1908 there was a food shortage in Japan, which resulted in the development of ophthalmia in a large number of children of the poorer classes. The popular treatment for this condition in Japan was the consumption of chicken liver or eel fats, both of which are rich in vitamin A. Recent research seems to suggest that many forms of infective disorders, more particularly infections of mucous membranes, may be due to lowered resistance to bacterial invasion consequent upon a deficiency of vitamin A in the diet.

Beriberi is the classical example of a disease due to a specific defect in diet, namely, deficiency in vitamin B_1; and pellagra, a disease the causation of which has been the subject of considerable research in U.S.A., is now regarded as being due to the consumption of a monotonous diet consisting of highly refined food which is deficient in vitamin B_2. Rickets and defective tooth formation are now known to be associated with an inadequate supply of vitamin D and it would seem that the adequacy or otherwise of the vitamin D content of the diet may depend to some extent upon the supply of other dietary factors. Scurvy is due to a deficiency of vitamin C and goitre results from lack of iodine in the food.

This brief summary of definite disorders known to be due to specific defects in

diet may serve to justify the importance of a proper diet, but it by no means represents the whole story. Various degrees of ill-health and unfitness, falling short of the actual fully developed diseases just mentioned, may result as a consequence of inadequate supplies of essential substances in the diet, and these conditions may be widespread and their nature and causation unrecognized. An instance of this kind in a large preparatory school has been described by Sir Frederick Gowland Hopkins. During the winter at this school, the standard of work and play fell much below normal, the boys became listless and irritable and their general condition was far from satisfactory. The ordinary hygienic environment at the school was good, and nothing was left undone in this direction but, nevertheless, the condition of the boys grew worse. Ordinary observers would have asserted that the diet was satisfactory and that the boys were well fed. On inquiry, however, it was found that the diet contained nothing in the way of uncooked food and practically no green vegetables. A small fruit shop near by from which the boys had normally supplemented the school diet with fresh fruit had been closed for some time. A liberal supply of fresh fruit was then provided and the whole trouble disappeared. The boys were suffering from unrecognized incipient scurvy.

When such a specific defect exists in the diet, it is probable that in the first place the body endeavours to bring its metabolism into equilibrium at a lower level, but if the deficiency is of such magnitude that this is impossible, a progessive deterioration of metabolism ensues which depends in degree and rapidity upon the extent of the dietary deficiency. This disordered metabolism eventually manifests itself in signs and symptoms which at first may be slight and indefinite, but eventually progress and develop into a symptom complex which is easily recognizable and can be described and named. Such well-known deficiency diseases as rickets, beriberi and scurvy are advanced stages in a long train of disordered metabolic activity which in its early stages produces effects so slight as to elude all means of detection at present available.

But in addition to negative factors in the diet which cause disease through lack of some substance essential for proper nutrition, there may also be positive factors in the shape of substances present in certain food materials which exert a definitely inimical effect upon metabolism and nutrition. Rickets and defective tooth formation are examples of disorders whose causation or prevention depends upon the interplay and resultant of both negative and positive factors.

The chief factor in the causation of rickets is deficiency of vitamin D in the diet. But it is impossible to say without taking into consideration other factors, what degree of deficiency is necessary to produce rickets. In other words, deficiency in regard to vitamin D requirements is not absolute but relative, and depends upon at least two other factors, namely, the supply of calcium in the diet and the extent and nature of the cereal constituents of the diet. Vitamin D controls the power of the body to retain and utilize the calcium in the food and if the supply of vitamin D is inadequate, then calcium retention is impaired. This can to some extent be corrected by greatly increasing the calcium intake ; calcification of bone is improved, but perfect bone formation is not to be expected merely by increasing the calcium supply when the supply of vitamin D is very small. When the amount of vitamin D is very small, the form in which calcium is administered has significance. Calcium carbonate is effective, but calcium phosphate has little or no beneficial effect.

Conversely, when the supply of vitamin D is adequate or abundant, then the utilization of calcium in the diet in any form, even as calcium phosphate, is very efficient and quite moderate supplies of calcium will ensure perfect bone formation. In other words, in order to obtain good calcium retention and satisfactory bone formation an abundant supply of vitamin D is far more important than abundant calcium.

In addition to these two negative or deficiency factors there is a positive factor

which may influence the production of rickets. This factor is a substance of unknown composition occurring in cereals, which exerts a powerfully inimical effect upon calcium retention and the calcification of bone. This rachitogenic agent or "toxamin" as it is called, is found in cereals and the germ of cereals, such as maize, barley, wheat, rice and oats, and of these oatmeal is the most inimical, in spite of the fact that it contains more calcium and phosphorus (both elements necessary for bone formation) than the other cereals. The anticalcifying effect of the toxamin of cereals can to some extent be neutralized by ample supplies of calcium, the carbonate being more effective than the phosphate. But the power of calcium salts in this respect is strictly limited. On the other hand, vitamin D has a powerful neutralizing effect upon the cereal toxamin and an adequate supply of it in the diet will ensure effective calcium retention and proper bone formation in spite of the presence of cereals and their toxamins in the diet.

The bearing which this interplay of factors has upon nutrition in ordinary life is important. Vitamin D is not widely distributed in nature and it is found most abundantly in only a few food materials which are, unfortunately, relatively expensive. It occurs most richly in the liver of fishes (cod-liver oil) and throughout the flesh of fatty fishes such as herring. It is also found to a lesser extent in egg yolk, milk, and dairy produce derived from milk, such as butter. The amount in milk is variable; sometimes it is very small, the content apparently being greater when the cows are kept under conditions which ensure abundant insolation. The amount present in butter varies *pari passu* with that in the milk from which it is made. Consequently it might be expected that butter made in countries such as New Zealand, where the cows live in the open throughout the year, would be richer in vitamin D than butter made in countries where cows spend a considerable part of the year in cowsheds. But milk contains a large amount of calcium: consequently conditions for calcium and vitamin D interplay are favourable and any vitamin D which the milk contains can operate at full efficiency. If therefore the diet contains a generous amount of milk it is probable that the supply of vitamin D will be adequate in most cases for the needs of the body. When a diet contains a large proportion of cereals there is a possibility that its vitamin D content, which might otherwise be adequate, may be rendered inadequate. There is therefore a real risk that many of the diets in vogue in this country where the antirachitic action of sunlight is insufficient to reinforce adequately the supply of vitamin D in the food, may be in the danger zone so far as an effective content of vitamin D is concerned. A remedy which has been suggested is that cereals in the diet should be restricted. Such a view, however, does not take cognizance of the fact that the energy supplied by the diet is at least as important as the vitamin supply, and cereals afford the cheapest, most readily obtainable and most satisfactory source of energy. The grain of cereals is intended as food for the young cereal plant, man has diverted it to his own uses and must consequently make the best of the advantages and disadvantages which such a material possesses when utilized for human food. After all, cereals must constitute a large part of the diet of man and as such must be accepted. Instead of condemning them because they may be unsatisfactory in certain respects, cereals should be utilized in combination with other foods capable of compensating for the disadvantages which they possess. The foods most suitable for this purpose are milk and fatty fishes such as herrings, and the increased consumption of these articles of diet is strongly to be recommended. It is now possible to reinforce the vitamin D content of food by adding to it artificially prepared vitamin D, i.e. ergosterol irradiated with ultra-violet rays or simply to irradiate food itself when any ergosterol which it may contain will be converted into vitamin D. Actually at the present time there is on the market margarine to which both vitamin A and vitamin D have been added, with the object of making the margarine approximate more closely to butter as regards nutritive

value. In the present state of knowledge it is not possible to say that such a product is comparable in all respects with butter so far as nutritive value is concerned, but it can certainly be said that margarine to which the above addition has been made is superior to ordinary margarine as a food. Milk has been irradiated and this treatment undoubtedly increases its vitamin D content. It is, however, open to the objection that irradiation may possibly affect adversely other constituents of the milk. If, therefore, it is desired to increase the vitamin D content of milk, it is preferable to add a known amount of irradiated ergosterol rather than to subject the whole of the milk to irradiation.

I have dwelt rather insistently upon the disorders (rickets and defective tooth formation) which result from an upset in the balance between vitamin D and certain other constituents of the diet, not only because these diseases are important and far reaching in their results, but also because the mechanism of their causation illustrates clearly that correct dietetics implies a delicate and complicated balancing of a variety of factors. It is unnecessary to multiply instances by detailed reference to other diseases caused by subtle defects in diets, such, for instance, as beriberi, pellagra and scurvy. The facts are sufficiently well known. But it is obvious that, involved as are the considerations which have been discussed with regard to vitamin D, the problem becomes infinitely more complicated when other possible deficiencies, together with positive inimical factors and their interactions, are contemplated. It would seem as if the ultimate problem of a completely satisfactory diet would defy solution. It may be so; mankind has to make use of the food materials available to him, and it is possible that no perfect diet can be contrived, and that all that can be done is to ensure a diet which, for practical purposes, and under the conditions in which we find ourselves upon this earth, shall be as near the conceptually ideal diet as can be attained. Fortunately, in practice, it is not difficult to utilize available foods so as to obtain satisfactory nutritional results. It might be possible to construct a mixed diet, consisting of the commonly utilized classes of foods (seeds, tubers, roots, and meat) in such a way, and in such proportions, as to supply just enough of each constituent necessary for nutrition. But in any such diet there would be danger of shortage of at least two vitamins, vitamins A and D. At the best such a diet would be perilously near the border line of safety and might place the consumer in what has been called the "twilight zone," within which a very slight change in any of the dietary constituents may cause an important shift of balance in the wrong direction. We have seen how in the case of vitamin D, adequacy in respect of one essential constituent may be converted into inadequacy when the balance in respect of some other constituent of the diet is altered. It is evident that it is impossible to say what is the safe minimum of any dietary factor, unless the biological values and interactions of all other constituents of the diet are known, and in the present state of knowledge this is beyond our powers. When the constituents of a diet are such as to bring the consumer into the so-called twilight zone, any small shifts in the quality of the diet, with respect to any factor, may either stabilize the processes of metabolism, or may lead to abnormal and pathological results. There are two foodstuffs which are capable of shifting the balance of practically any ordinary mixed diet into definite stability; these are green vegetables and milk. Green vegetables ensure an adequate supply of vitamin A, and milk, in sufficient amount, provides the vitamin D and calcium necessary to raise the diet into the region of safety. It would appear, therefore, that where a diet is supplemented by milk and green vegetables, the other food materials may quite satisfactorily consist of articles which are easily obtained and relatively cheap, such as flour and its products, bread, etc., the pulses (peas, beans, lentils), potatoes and roots, such as parsnips and carrots, sugar and fat of all kinds.

The value of milk as an article of diet consists not only in its vitamin and

calcium content, but also in its other constituents. The protein of milk is of high biological value, and in addition to this, milk would seem to have some other specific nutritive qualities not yet understood, which put it in a class by itself as a food of special value for proper nutrition. It is pardonable to adapt Goethe and say of it "Milch ist ein ganz besondrer Saft." Nor is this to be wondered at when we reflect that milk is the only food which has been specially designed and constructed for mammalian nutrition. All other materials used for food are primarily contrived to other ends, and are only secondarily mammalian foods, having been pressed into this service to meet nutritional needs.

In regard to meat, "offal," such as liver, is rich in vitamin A and vitamin B, and to this extent would appear to be superior to skeletal muscle (ordinary meat). Herrings are a cheap means of still further enhancing the supply of vitamin D in the diet.

Another aspect of nutrition is the possibility of damage to important constituents of food as a result of processes which food may undergo in its preparation for consumption. Perhaps the most obvious example is the complete destruction of vitamin C, which occurs when vegetables are dried; no reliance can be placed upon such vegetables as a preventive of scurvy.

Until recently it was thought that the canning of fruit and vegetables necessarily resulted in the destruction of vitamin C. The destruction of vitamin C is an oxidative process which occurs rapidly when foods containing it are heated in the presence of air or oxygen. In the modern improved methods of canning, however, precautions are taken to exclude air as far as possible, so that in most cases less destruction of vitamin C may be expected than when the foods are cooked in the ordinary way in open air.

It has been found that tomatoes and fruits which contain little oxygen are very slightly affected in respect of their vitamin C content by canning; canned tomatoes and canned peas contain rather less vitamin C than orange juice. Canned cabbage, peas and spinach have been shown to be actually richer in vitamin C than cabbage, peas and spinach cooked in the ordinary way. Apples as a class are relatively poor in vitamin C, with the curious exception of the variety known as Bramley's Seedling which has definite antiscorbutic properties only slightly impaired when this apple is cooked in its skin.

The pasteurization of milk is now widely practised, with the object of improving its keeping qualities and destroying any pathogenic organisms which it may contain. The chemical and physical properties of milk are not perceptibly affected by a temperature of 145° F., with the exception that a small portion of the calcium—only about 2%—may become indiffusible and some of the small amount of vitamin C which milk contains may be destroyed. There is also a slight change in the rate of coagulation by rennet. The degree of destruction of vitamin C during pasteurization appears to depend upon the metal of the vessel in which the milk is heated. Aluminium for example has a much less destructive action than copper. A number of observations have been made with a view to ascertaining whether pasteurization affects the nutritive value of milk in any way; divergent experiences have been reported, but no results have yet been obtained which can be accepted as definitely conclusive one way or the other. If there should be any difference in nutritive value between ordinary and pasteurized milk it would seem to be small, and for infant feeding probably less than the difference between cow's and human milk. However this may be, the protection against bacterial disease conferred by pasteurization may be pleaded in support of the practice.

It is generally recognized that milk obtained from perfectly healthy cows, under the cleanest conditions, cooled immediately and distributed with the least possible handling and delay, is the best that can be procured. The difficulty in existing circumstances, however, of securing such ideal conditions for milk production

inevitably restricts the supply. In a highly urbanized country such as England transport and distribution complicate the problem of a satisfactory milk supply, and in order that an adequate, safe, cheap supply of milk should be readily available for everyone, it is necessary to have recourse to pasteurization. But pasteurization must be properly done if milk is to be rendered safe, its keeping qualities improved and its nutritive properties not appreciably affected.

It is, however, not possible to justify on similar ground of expediency certain other food manipulations. The bleaching of flour, for instance, has for its object the removal of the golden yellow colour natural to many wheats, in order to produce a flour of a uniform degree of whiteness which the consumer is said to demand.

The recent Departmental Committee on the Treatment of Flour with Chemical Substances considered this question from three points of view: (1) what takes place in the flour when it is treated with bleaching agents; (2) what, if any, toxic effect each may have on the consumer directly by itself or in combination with some constituent of the flour, and (3) what, if any, effect each may have on the nutritive properties of the flour. The committee pointed out that chlorine, for instance, oxidizes the colouring matter of the flour, carotene, into a colourless compound, that it enters into combination with the oil of the flour probably forming chlorine addition products and that chlorine could act upon gluten. This interaction with gluten includes the entrance of chlorine into such important parts of the gluten complex as the tyrosin and tryptophane groupings, with injurious results so far as the nutritive value of the gluten is concerned. The committee realized that it might be urged that the amount of chlorine used is relatively small and that any changes which may be produced in the flour may also be small and for practical purposes may be disregarded. They considered this to be a dangerous argument, since it is known that foodstuffs contain substances which may be present in very small amounts but are of the highest importance for proper nutrition. These substances are very susceptible to mere traces of chemical reagents which may alter or destroy them and so irremediably impair the nutritive value of the food which contained them. The absence of obvious symptoms in the consumer of such food cannot be regarded as evidence that the food is certainly innocuous or that its nutritive properties have not been damaged in some subtle but important respect. Obvious symptoms are merely the summation of a long series of subtle metabolic changes which by themselves elude our present imperfect methods of detection. It is quite possible that the composition of a food material might be so altered in an adverse direction that, although the body would be capable of dealing with it, an extra strain would be imposed upon the tissues and cells which they should not be called upon to bear.

Such then was the opinion of the committee, although they were not able to assert categorically that the destruction of carotene in bleaching had a demonstrable significance in nutrition. It has, however, been shown recently that when carotene is fed to an animal it would seem to be converted into vitamin A in the liver, in fact, carotene appears to be a precursor of vitamin A. If these findings are confirmed, the presence of carotene in flour assumes an importance which it was not possible before to ascribe to it. The bleaching of flour destroys a substance upon which the body relies for a part, at any rate, of its supply of vitamin A. It is true that the amount of carotene in flour is small but flour forms a large part of most diets and it may be that a significant proportion of the body's requirements of vitamin A may be derived from it. If this be so, the committee's distrust of the bleaching of flour—based upon the general trend of knowledge is confirmed—and justified.

Another food manipulation which has recently assumed prominence is the treatment of fruits and other foods with hydrogen cyanide for the destruction of insect life. Apart from any question of the possible toxicity of traces of hydrogen cyanide or resulting cyanhydrins which may remain in the food after treatment, hydrogen

cyanide exerts an inimical action on the living cells of fruit subjected to its action. This action is apparently closely associated with a paralysis of the cells' respiratory mechanism which depends upon the interaction of oxidases, cytochrome, and other agents concerned with the supply of oxygen for respiration.

In addition to the commercial damage and loss which may result from over-treatment of fresh fruit and vegetables, there is the further question whether it is desirable on health grounds that foods should be subjected to indiscriminate treatment with hydrogen cyanide. It is generally agreed that fresh fruit and vegetables are of importance in the dietary, quite apart from their vitamin C content. It is possible that some factors associated with the living plant are essential to health. Fumigation with hydrogen cyanide, unless carefully regulated, interferes with processes upon which the vitality of the plant-tissues depend, but present knowledge does not permit us to say definitely whether any change in composition may occur which may impair the nutritive value of the food.

It may be objected that in many cases the changes in composition caused by food manipulations are so small that they cannot be of any great importance in nutrition. From a purely chemical standpoint such changes may be insignificant, but from the standpoint of metabolism it is possible that some of them may have profound significance. The needs of the body for iodine can be satisfied by minute amounts of this element, but if these necessary traces are lacking in the food, grave disorders of metabolism ensue. Acetyl choline is an essential substance for the regulation of the heart-beat, but the amount needed is excessively minute ; a concentration in the blood so extraordinarily dilute as 2×10^{-12} or 1 milligram in 500,000 gallons will produce a definite effect upon the heart. These are only two instances amongst many ; in fact, biological research tends more and more to emphasize the importance of "the infinitely little" in the processes of metabolism.

It would seem that during the long ages of evolution, living tissues have pressed into the service of nutrition a variety of materials which they have found in their environment, and that their scheme of metabolism has developed along such lines as make it absolutely dependent upon a supply of these materials. And when such a fundamental characteristic as a metabolic process has once been established, it is not readily put aside or modified to meet a changed environment. When life was passed in the sea, the traces of iodine in sea-water were utilized in the scheme of metabolism which was then evolved, and the need for iodine has persisted to this day in those animals which have forsaken the sea for a land existence. Never before the advent of man have animals possessed the intelligence necessary to interfere with the composition of their food environment. A great responsibility therefore attends the manipulation of natural foods, and if this is not recognized it may be at our peril that we meddle. Knowledge wrongly used may well justify the warning that "with much wisdom cometh grief and he that increaseth knowledge increaseth sorrow."

In conclusion I would stress the belief that in proper nutrition we possess a most powerful environmental means for attaining sound physical development and resistance to disease. Too many children enter their school life already handicapped by defects, such as stunted growth, abnormal tissue development, defective teeth and infections of mucous membranes, all of which we know to be closely associated with imperfect nutrition. The means of prevention are to hand ; they are simple and are infinitely less costly than the results of supineness or misdirected effort.

Discussion.—Sir GEORGE BUCHANAN, disclaiming any authority on questions of dietetics, said that the value of Dr. Hamill's paper seemed to lie, not only in philosophical outlook, but in the opportunity it gave to experts to deal with controversial matters like the nutritional value of pasteurized milk as against raw milk, or the effect on cereals of bleaching by chlorine and fumigation by cyanide gas. In so far as such questions, and many others raised by Dr. Hamill, depended on the reduction of different vitamins, should not a practical distinction

be made between the requirements of the growing child and the needs of the ordinary adult taking the ordinary mixed diet customary in this country? He did not mean only those who could afford, and habitually took their food and drink in plenty of variety; he would include those who, for economic reasons—unemployment and like causes—had a relatively monotonous and necessarily cheap diet. There were a few quite special cases during the war, for example in Mesopotamia, where the extreme restriction did in fact produce deficiency diseases. But an important question for the adult population of this country at the present time was whether the customary diet of the individual, even in hard times, was so close to the margin of vitamin deficiency as to endanger health from the mere fact of that deficiency. When they spoke of insufficient food or malnutrition, should they think principally of the quality and quantity of the food, or give first attention to the proportions of vitamins? The latter, seemingly, were only needed by the adult in very minimal quantities.

Sir WILLIAM HAMER said that the study of the infinitely little in metabolism was most intriguing, and the experiences they had all gone through in the winter of 1917-18, when they had had first hand experience, even on a mild scale, of the effects of shortage of food, must have convinced them that the questions raised in the paper under discussion were most important. The effect of such privation, as was felt at the close of the Great War, upon lowering resistance to infectious disease in rationed and segregated communities, particularly in large towns, had especially impressed him at the time, and he looked upon these experiences as being highly significant, from an epidemiological point of view, and as throwing much light upon epidemiological history relating to war and famine fevers in earlier centuries.

Dr. KINGSTON BARTON, referring to rickets, said that in the 1880 decade the prevailing opinion was that the early and too free use of starch in the dietary of suckling infants was the chief factor in the cause of this disease. For a good many years that had been ruled out. However, from what Dr. Hamill had said, and from what Professor Mellanby and other workers had written, it was now admitted that the cereals seemed to contain some element that tended to produce rickets. The once much-vaunted Scotch porridge was now held to be the worst sinner amongst the cereals. Although we might be said to have gone back fifty years in this matter of the starch component of infant feeding, yet we must thank modern progress for its contribution in this knowledge of the various vitamins.

Dr. W. CRAMER said it was particularly important to recognize, as Dr. Hamill had done, that the so-called deficiency diseases were only the termination of a gradual deterioration of health, resulting from an imperfect diet. This gradual deterioration of health produced conditions which were difficult to recognize, especially in an adult person, because its manifestations were elusive and manifold. These conditions, which could not be called "a disease" and which he (the speaker) had described as "the borderland between health and disease," had nevertheless a definite pathology (atrophy of mucus secreting cells in the mucous membranes of the respiratory and digestive tract when the supply of vitamin A was inadequate; atrophy of lymphoid tissue when the supply of vitamin B was inadequate). Inadequate diets produced these pathological changes in the adult organism as well as in the young and growing organism. The question had been raised in the discussion whether the adequate supply of vitamins was as essential for the adult organism as for the growing one, and this question was often answered in the negative. The experimental evidence, however, demonstrated conclusively that the adult organism could not maintain its health without an adequate supply of vitamins, with the exception of vitamin D which seemed to be necessary only for the growing organism to assure normal bone formation when the inorganic materials for bone formation were not supplied in the food in the proper proportion. The reason for the view that the young and growing organism was particularly dependent on the presence of vitamins was that in that case any deterioration of health manifested itself by a retardation or arrest of growth. Subnormal weight and retarded growth were warnings that the organism was in the borderland between health and disease and that the diet might be inadequate, and when a definite disease, e.g., an infection, eventually set in, the two events were correlated. In the adult organism there was no such obvious danger signal, and any infection which occurred appeared simply as an infection and nothing more.

The multiplicity of vitamins which recent research had demonstrated might lead one to think that it was a difficult problem to formulate an adequate diet. This, however, was not so. One might take it as a golden rule that any diet which was built up around a basal ration

of fruit, cereals, and milk or its products—butter and cheese—fulfilled most dietetic requirements. There were, however, two difficulties in the way of the practical application of this rule. Cereals, which ought to be the main source of supply of vitamin B in the diet, were consumed in this country mainly in the form of white bread, which was completely devoid of vitamin B. This error could be readily corrected by the consumption of one of the numerous kinds of wholemeal bread or germ bread now available, which were rich in vitamin B. The difficulty concerning the supply and consumption of milk was more serious. He had calculated that the average diet required for each individual, young or adult, the inclusion of half a pint of milk and an ounce of butter. This was at least double the amount actually consumed in this country on the average. But if an attempt were made to remedy this condition there would not be enough milk available to satisfy the requirements. The only remedy at present was to provide a margarine containing vitamin A, as a substitute for butter. Another difficulty was of an economic nature. Milk and butter were relatively expensive articles of diet. He was convinced that more varied forms of ill-health could be traced to dietetic inadequacy, and especially to the inadequate consumption of milk and butter than was at present realized.

Dr. S. MONCKTON COPEMAN said it was of interest to recall the fact that our knowledge of "accessory food factors"—as they were originally termed by Professor Sir F. Gowland Hopkins—had been built up practically within the present century. Before that time it was believed that so long as a correct proportion was observed with regard to the various classes of food-stuffs, and that a sufficiency of these in combination was supplied to ensure the intake of the requisite amount of calories, nothing more was necessary. In spite of all our present-day knowledge, however, he (Dr. Copeman) was of opinion that sufficient attention was not always paid to what he would term the "æsthetics" of nutrition, by which he meant that palatability of food and the artistry of its preparation and presentation was undoubtedly capable of exerting an important influence, in part by creating and stimulating appetite and also by aiding digestion. Empirical knowledge of this factor was enshrined in the remark of a working-class woman in the Midlands who, when questioned as to her household budget, said that she always tried to give her husband "a relish with his tea."

In this connection it might be worth while to stress the value of watercress as a tasty and valuable addition to the small list of vegetables eaten in an uncooked condition; this salad plant contained not only vitamins in considerable amount, but also much chlorophyl, together with iodine and iron in small quantities, in addition to a volatile, oily, sulphur-containing body to which the peculiar flavour and smell of watercress was due—consequently, although of practically no actual food-value owing to the large content (93-95%) of water, this plant possessed valuable tonic and stimulant properties. Indeed, as Dr. Corry Mann had shown, excellent results, especially in the case of ill-nourished children, had been observed to follow on the addition to their food of a daily ration of watercress.

[In conclusion, Dr. Copeman referred to work carried on at the London Zoological Gardens in regard to the most desirable composition of the dietaries of the various animals in the collection, more especially the large carnivora. As an interesting and valuable outcome of this work, a number of healthy lion cubs had been bred there during the past year or two, whereas formerly any that were born there soon died, with symptoms of "deficiency" disease, usually developing in the form of rickets.]

Dr. CORRY MANN said it was an undeniable fact that in many large cities housing conditions in congested districts had altered little in the course of twenty-five years. In the South London riverside zone, between Westminster Bridge and the Surrey Commercial Docks in Rotherhithe, in thousands of tenements and houses at the present day were found the same occupations of wage-earners, the same prevalence of casual labour and the same density of population—as shown by the average number of persons per room. Yet there was year by year a steady fall in morbidity and mortality rates during childhood, and the average child of any given age was taller and more healthy than such a child in the years before the European war. That an improved food supply throughout the year had been partly responsible for an improvement in nutrition was suggested by the changes seen in the type of case admitted to the wards of hospitals for children. In the first place, abdominal tuberculosis was rarely seen now, and the cases of that disease which were admitted usually came from country districts, where milk was not pasteurized. Secondly, we were no longer harassed by an appalling mortality from

epidemics of summer diarrhœa during the months of July, August, and September. Raw milk supply had been made safer by pasteurization, and as the supply of pasteurized milk had increased, so the incidence of these two diseases had diminished. A question had been asked as to whether the nutritive value of milk was impaired by the pasteurization process. He could find no clinical evidence of this. For five years past pasteurized milk had been used in his wards, without any protective antiscorbutic ration of orange juice, for babies under the age of two years. Furthermore, growth rate had been regular, and radiography had shown no evidence of deficient calcification in bone-forming cells, indicating that the slight precipitation of calcium which occurred during the process of pasteurization was of no importance so far as nutrition was concerned.

Another improvement in food supply enjoyed by the present generation, was in the matter of fruit, the marketing of which was much more continuous throughout the year. He was not speaking of luxury fruit, but of the orange and the apple, the supply of which to industrial districts was no longer confined to the English and American apple harvest and the South European orange crop. All the Dominions, Jamaica and Brazil now exported one or other of these fruits, and he believed that the increased fruit importation to this country was a factor in producing a fall in morbidity rates during childhood.

In Mr. J. Sim Wallace's opinion the principal cause of dental caries was deficient cleansing of the teeth in association with sugar lodging about the crevices and retention areas of the teeth. This view had received support from observations which he (the speaker) had made a few years ago during a dietetic investigation of boys of school age living in an institution near London. Though the basic diet was low in caloric value, and only 18% of the calories were in the form of fat, and though the diet was undoubtedly deficient in vitamins A, C and D, yet practically no dental caries was seen. This he attributed to efficient dental supervision, strict routine toothbrush drill and the fact that the boys, having no pocket money, could not obtain sweets, the only extra rations being fruit and plain cakes. He agreed with Mrs. Mellanby that a dietetic deficiency was responsible for the rapid caries and disintegration of teeth occurring between the ages of 20 and 30.

With regard to the dietetic requirements of a healthy adult, after the growing age had been passed, the caloric requirements of an adult labourer out of employment should be satisfied by 55% of his diet during full work, and 2,100 calories should enable him to maintain an average weight, to take a necessary amount of exercise, and to avoid deterioration in health, provided that the diet was of suitable balance and quality.

Dr. HUGH STANNUS said he had been greatly interested in the paper and discussion, as for a number of years he had been living in contact with native races in Africa among whom the problem was a very real one—many whole tribes lived in what Dr. Hamill had described as "the twilight zone." It was necessary to study these problems from a wide angle. For instance, he had shown many years ago that rickets did not occur among native children, though they were literally stuffed with cereal food from the first week of their birth. They were breast-fed for two years, had ample chance of moving their limbs, and a plentiful supply of sunlight. Their supply of vitamin was sufficient to protect them from the ill-effects of rachitogenic factors in their diet.

As Dr. Cramer had pointed out, there was always a fashion in medical thought. He would like to suggest that the fashion of thinking of the so-called "deficiency diseases" in terms of lack of vitamins was hindering progress. The symptoms in many of these diseases, rickets, pellagra, and beriberi, to mention those he was most familiar with, were of a "positive" nature. He could understand negative symptoms being due to a deficiency but it had always appeared to him that where "positive" symptoms existed one should look for positive factors in the ætiology which were perhaps unmasked by a lack of vitamins. Dr. Hamill had only briefly alluded to this positive factor in rickets—the toxamin contained in oatmeal and other cereals. He believed that similar toxamins would be discovered in pellagra and beriberi. In other diseases it might be a virus, toxin, or ferment which was allowed to come into action. Research on this side of the problem was much needed.

He thought there were many conditions associated with ill-balanced diet and deficiency in vitamin content apart from well-defined clinical entities, which could be observed if looked for.

Fleet Surgeon W. E. HOME said that it was difficult to recognize deficiency diseases when they were just beginning. Dr. F. v. Hahn had a paper on "Vitamin-therapie" in *Medizinische*

Welt, p. 664, in which he gave as the earliest signs of scurvy (as Lind had done 150 years ago), easy fatigue and distaste for work, then, later, disordered appetite and pains in the joints, and later still, hæmorrhages from the gums or elsewhere. He found at Hamburg a maximum death-rate in December, and another, a little lower, in March, when he thought that the want of vitamins was at its worst; this March maximum did not appear in London. Families of poor people were healthier in spring if they had a garden (allotment). Hahn had said that school-children in April suffered from conjunctivitis, which was apt to be ascribed to over-work before examinations, but was curable with cod-liver oil, being really a xerophthalmia.

Dr. J. D. ROLLESTON, asking for some information about the vitamin content of the commonest alcoholic beverages, said that a French medical audience would probably have been surprised that no reference had been made by Dr. Hamill to alcohol as an article of diet. At the present time an intensive campaign, in which even the Professor of Therapeutics in the Paris faculty, Dr. Maurice Loeper, was taking part, was being carried on in France on behalf of the alimentary and therapeutic value of wine.

ALQUIER, J. et LOEPER, M. Le valeur alimentaire du vin. Rapport presenté au Comité international du vin, *Progrès méd.*, 1929, xliv, 1637. LOEPER, M. et ALQUIER, J., L'action physiologique et thérapeutique du vin, *ibid.*, 1725. See also AUBERT, E., L'épreuve du vin chez les hépatiques, *Thèse de Paris*, 1930, No. 279.

Section of Laryngology.

President—Mr. FRANK A. ROSE, F.R.C.S.

[*November* 7, 1930.]

DISCUSSION ON PRECANCEROUS CONDITIONS OF THE LARYNX.

Dr. Chevalier Jackson (U.S.A.): This subject is of the utmost importance from the viewpoint of the study of the problems of ætiology, prophylaxis and treatment of the "dire disease," as the late Sir Henry Butlin called cancer of the larynx. The subject might conveniently be considered under the subheadings of (1) the word; (2) the condition; (3) the question as to whether such a condition is recognizable; and (4) the treatment.

(1) *The word* is faulty; much time has been wasted in discussions from lack of beginning with a definition; the participants were not talking about the same thing. If we use the word to mean a stage always traversed in the transition from the normal to the neoplastic, it is doubtful that we have sufficient evidence to justify its use. If we use the word as meaning only a soil favourable to the development of cancer, little fault can be found and discussion will be useful.

(2) *The condition* of the tissues previous to the development of cancer might hypothetically be described as a preparation on the part of the cells to do something not already done. Metaphorically, it might be described as a large number of the citizens across the border leaving their regular daily routine and mobilizing preparatory to invasion. Similar misbehaviour on the part of the cells that have not yet crossed the border is often seen adjacent to an area where invasion constituting cancer has already begun. Occasionally it is seen without any subsequent invasion. Any inflammatory or irritative condition in the larynx might be called precancerous, but such use of the term would be a very loose application indeed.

(3) *Is it recognizable?* Perhaps very rarely, as a histologically proven fact. To ask the histologist to tell us, from the examination of dead removed cells, what adjacent living, unremoved cells are going to do, is asking much, yet occasionally this has been done on the basis of probabilities. An illustrative example was published by me in the *Proceedings of the American Laryngological Association* for 1922. Sir StClair Thomson, Mr. Herbert Tilley, the late Mr. Hunter Tod and myself, from mirror examinations, believed that the condition in the larynx of a man aged 42 years was suspicious. Histological examination by Dr. James Ewing demonstrated a cellular structure to which the term *precancerous* could conveniently be applied, inasmuch as the deeper cells were misbehaving and showed a sudden transformation of the normal to hyperplastic and atypical epithelial pegs, but they had not yet invaded the submucosa. Dr. Ewing added the comment: "This is the stage in which to treat cancer of the larynx, not after it gets well advanced." Laryngofissure, with moderately wide removal, completely cured the condition, and the patient is in good health with a good voice, after 14 years. In contrast with this case are those in which a chronic laryngitis is followed by a stealthily developing cancer after many years, as long as thirty in some of my cases. A precancerous stage may exist in such patients but clinically it is unrecognizable.

(4) *Treatment.*—The clinical indications for treatment are clear, though not always easy of accomplishment. Every curable disease of the larynx and upper air passages should be cured, and all incurable conditions should be ameliorated so far as possible. Avoidance of all forms of laryngeal irritation is imperative. Vocal rest and avoidance of alcohol and tobacco should be insisted upon. At the first sign of cancer a biopsy should be made; further treatment should be based upon histological findings.

Sir StClair Thomson said that he, too, would ask the question: Was there such a thing as a recognizable precancerous condition of the larynx? We had to distinguish between predisposing conditions and precancerous conditions. The only predisposing conditions known were sex and age. He had never convinced himself that there were local predisposing conditions. He had not met with cancer of the larynx more frequently in voice-users than in others, or in those subject to chronic laryngitis, or to cough, or in those who had suffered from innocent growths, or in those who had undergone frequent endolaryngeal manipulations. He had not been impressed with the idea of syphilis, tobacco or alcohol being factors in a precancerous condition, though they were so potent in causing chronic laryngitis. In ten out of his eighty cases of laryngofissure the patients had been women and they had never smoked or touched alcoholic liquors. Of course it might be quoted that in many cases of extrinsic cancer—the post-cricoid form chiefly—in women, it had been noted by independent observers that the patients had complained of some swallowing difficulty for years.

It was somewhat risky to argue on grounds of analogy, but many years ago the question of a pretuberculous condition was raised, but it had now, he thought, been abandoned. The analogy was not a suitable one, because tuberculosis resulted from a definite infecting organism. No organism, no tubercle. In the case of the breast there was the analogy of the early condition of the nipple. One knew about the lip condition in smokers, and about the conditions in chimney-sweep's cancer, but did malignant disease in the rectum occur more frequently in those who had rectal troubles, such as hæmorrhoids? Had Members not been struck with the fact that cancer of the œsophagus did not occur particularly in people who had had trouble with the mouth or the pharynx, or other supposedly predisposing condition? He had read that cancer of the stomach did not affect the dyspeptic person, but rather came "like a bolt from the blue."

As to innocent neoplasms, though, as Dr. Chevalier Jackson had wisely said, every person of middle age, with a lesion in the larynx, should be suspected to have malignant disease until proved otherwise, yet such a condition might be innocent. He had seen a man, aged 62, who for two years had had a typical cupped infiltration in the centre of one cord. He had pus in one antrum, and was referred back to his laryngologist for treatment and further observation. Two months later he came almost free from catarrh and with a voice almost normal. Where the cupped condition had been there was a small fibroma. But the patient had lived many years, and had died from a different disease.

Out of eighty laryngofissure cases he, Sir StClair, had twice made a mistake in diagnosis. The first was in the case of a patient, who, at the age of 51, had been husky for eighteen months. She tried treatment by silence for a month. The lesion was not suitable for the removal of a piece for biopsy, and, after some hesitation, a laryngofissure was decided upon. The larynx was opened, Mr. Colledge assisting, and he (the speaker) then pointed out the use of the finger as a test. This growth was soft to the touch, and he therefore felt that he had made a mistake; still, because of the patient's age, the growth was removed. The pathologist reported that there was no evidence of carcinoma anywhere. Several plasma cells and some infiltration were found. Was that a precancerous condition? Perhaps some day the pathologist might be able to distinguish between an innocent and a precancerous condition.

The second error in the series of eighty laryngofissures had consisted in mistaking tuberculosis for cancer.

He would now show a slide illustrating the case of a patient who had been husky for six months. On one cord there had been a typical malignant growth, and on the opposite cord a curious condition like a plaque. He (Sir StClair) had felt so suspicious that the man had malignant disease on the opposite cord that, when

dividing the thyroid cartilage he had kept well over to the less affected side. Microscopic sections showed typical malignant disease all along the diseased side. On the opposite side the condition, which had looked suspicious, was declared to be innocent. That patient remained well several years afterwards, though with a somewhat narrowed glottis.

In another case the patient, aged 62, had evident syphilitic scars on his tongue, though the Wassermann reaction was negative. He neither smoked nor took alcohol and his teeth were perfect. He was treated with large quantities of mercury and iodides, and had been seen by specialists in Berlin, Paris, Spain and other places. He presented the condition depicted in the slide [shown]. Professor Sebileau in Paris told him not to have it touched then, but to have it watched, as it might one day become malignant. After two years of watching, the man's voice had become so much impaired (preventing him from carrying on his business) that he (Sir StClair) began local removal, through the mouth, and finished it two years ago. The voice was now normal. Had that been a precancerous condition?

His (the speaker's) view was that no final conclusion on the matter had yet been reached. But, as a celebrated Frenchman had said, it was much better to discuss a subject without coming to a conclusion than to come to a conclusion without discussing it.

Mr. Lionel Colledge: Sir StClair Thomson has told us exactly how our knowledge stands but I feel that his cancerogenic nihilism would leave the mystery for ever unsolved. I ask your leave, therefore, to offer some speculative suggestions on how cancer originates in the larynx, and I apologize if they are not all strictly relevant to the larynx.

M. Auguste Lumière in a small book entitled "Le Cancer-Maladie des Cicatrices" has put forward the hypothesis that the common epithelial cancers originate in scar tissue. This excludes from consideration tumours which originate in embryonic rests, for example, inclusions in branchial arches, and the sarcomas originating in connective tissue. It includes all the epitheliomas as encountered ordinarily in the pharynx, larynx and œsophagus and on the tongue. If any advance in this branch of knowledge is to be made at present it is more likely to be found in studying the pathogenesis of particular groups of tumours than in studying that of tumours as a whole. It is unlikely, for instance, that a teratoma of the testicle and an epithelioma of the lip have an identical pathogenesis. It is therefore justifiable and necessary to limit ourselves to the discussion of epithelioma and even to a particular area.

The transition from simple papilloma into epithelioma can now be followed experimentally by the production of tar cancer, so that the true precancerous stage can be studied microscopically. The chief manifestations are epithelial hyperplasia with irregularity in the size, shape and staining properties of the cells, affecting the Malpighian layer. There is also hyperkeratosis and the keratinized layer sends prolongations into the Malpighian layer. There is also increased mitosis, but the basal layer remains intact and the stage is genuinely precancerous.

Professor Benjamins therefore claims that when a piece of tissue from a vocal cord shows such characters it is to be considered in a precancerous stage, since experimentally these characters have been demonstrated to be precancerous. How is the precancerous condition produced?

The part played by chronic irritation has been for many years vaguely but widely recognized and Lumière notes no less than 44 different types of epithelial tumour in which this can be traced as a predisposing cause. It is not necessary to enumerate these, but if we accept this as a hypothesis, two questions at once demand an answer. (1) Is this chronic irritation, with the production of scar tissue, an essential preliminary to the production of an epithelioma? (2) Why do some scars undergo a cancerous degeneration, whilst others remain free from such proliferative change?

In the first place, there are a number of situations in which epithelioma does not occur unless it is definitely preceded by chronic irritation and scar formation. The epithelioma which is seen in Kashmir as a result of a chronic burn on the abdominal wall from the use of braziers is the classical instance.

It is suggested that if we could only demonstrate it, the presence of a scar is a necessary preliminary in every case. It used to be considered that about 5% of gastric cancers were preceded by gastric ulcer, but the Mayos have shown that 70% have supervened on a previous simple ulceration.

It may be the case, therefore, that a pre-existing scar is necessary to the production of every epithelioma, and if it cannot always be demonstrated, the evidence of it may well have been destroyed by the growth. Also, the first condition for its demonstration is to look for it, and this is not always done. This argument requires to be elaborated in greater detail but it is a reasonable hypothesis that a scar is not merely a predisposing cause but an essential preliminary condition.

Secondly, why do some scars become cancerous? Where scar formation is, beyond question, a predisposing cause—as in the case of epithelioma appearing in the cicatricial tissue resulting from a burn—the wound has been slow in healing or, perhaps, owing to prolonged suppuration, has never healed at all.

Thirdly, the cancerous change does not occur as soon as the wound or ulcer has healed. Twenty or thirty years must usually elapse, so that it is the age of the scar, rather than the age of its host, which is important. The scar, if healed, must eventually be subjected to some secondary injury such as a blow or a fresh erosion.

This continuous but varying stimulus to cell formation produces a local tendency towards multiplication of cells, which revert towards the embryonic condition, but the differentiation does not go so far as this; they merely become rejuvenated, retaining the characters of the mother tissue. Thus metastases retain these characters. This may explain the failure of microbic and parasitic theories to account fully for all the phenomena of cancer. It does explain the age incidence of cancer and is compatible with various other points, such as the constant areas which include the sites of origin and the variations in radio-sensibility.

Professor Alfred Denker has reported the case of a man, aged 50, who was brought to the clinic suffering from severe stenosis of the larynx. He had attempted suicide twenty years before by cutting through his larynx with a razor. The wound healed eventually, leaving some difficulty in breathing, but he was able to do light work. For three months the difficulty in breathing had increased. There was a scar in the front of the neck firmly adherent to the cricoid cartilage. The vocal cords were almost fixed in the middle line and appeared heavily infiltrated and thickened. After a low tracheotomy a piece of tissue removed for examination showed carcinoma. Total laryngectomy was performed and it was found that the trachea was extensively invaded with growth, so that the upper part was resected in addition to the larynx. From subsequent examination Borst considered that the cancer definitely arose from the scar tissue.

[Mr. Colledge showed the larynx of a patient who had been gassed during the European war and had never recovered his voice. In 1925 a laryngofissure was performed but a recurrence proved by biopsy soon occurred and the whole larynx was removed ten months later. On the screen, the larynx was seen from below. The stenosis from scar formation, in which the recurrent epithelioma was situated, was well demonstrated.

Mr. Colledge also showed a picture of the œsophagus of a man who had suffered from achalasia for twenty years. About six months before his death he had a hæmorrhage, complained of pain in the side and began to lose weight, while the liver enlarged. At the necropsy the liver had weighed eleven pounds, owing to secondary deposits. The picture showed a huge epithelioma grafted on the dilated and diseased œsophagus.]

Nevertheless, even when all the conditions enumerated are present, the scar does not necessarily degenerate into an epithelioma. Is there, in addition, any general or constitutional factor necessary to convert the local process? Slosse and Reding have shown that in persons afflicted with cancer there is an abnormality in the regulation of the blood-sugar, tending towards hyperglycæmia. This hyperglycæmia is independent of the situation of the tumour and of its histological nature, and there is evidence that this abnormality is a precancerous condition and is common also in the relatives of persons with cancer. Slosse and Reding have found also that an abnormally high alkalinity of the blood is common in persons with cancer.

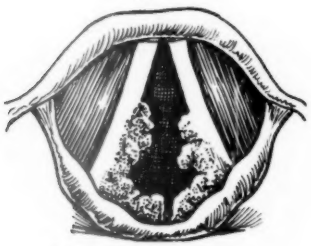
It is put forward therefore, with due acknowledgment to M. Lumière, as a basis for discussion, that the conditions predisposing to cancer of the larynx are: (1) The presence of scar tissue. (2) That the scar has been a long time forming or has never completely healed. (3) That it is many years old. (4) That some secondary injury or irritation occurs. (5) That some general factor is also present, probably a high content of sugar in the blood and an excessive alkalinity.

Mr. E. D. D. Davis showed drawings and microscopic slides of six cases to illustrate precancerous conditions of the larynx.

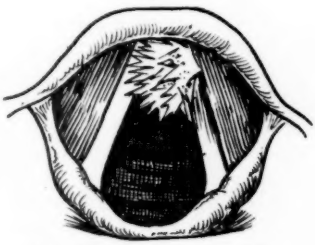
(A) A typical pachydermia in a man aged 57. Owing to laryngeal obstruction and the probability of malignancy, a laryngofissure was performed and the growth freely removed.

Section: Simple proliferation of the surface epithelium.

This patient was under observation for three years and no evidence of cancer appeared. He was thought to have pulmonary tuberculosis, but the tubercle bacilli could not be found in the sputum. Wassermann reaction negative.



A typical pachydermia.



A papilloma in a man aged 64.

(B) A white stalactitic papilloma of anterior third of left vocal cord in a man aged 64. Hoarse six months. Growth removed by laryngofissure July, 1923. Patient still well and no recurrence for seven years.

Section: Papilloma.

(C) A wet specimen of the larynx of an infant aged 20 months, with a single papilloma growing from the anterior third of the left vocal cord, almost identical with that in B (above).

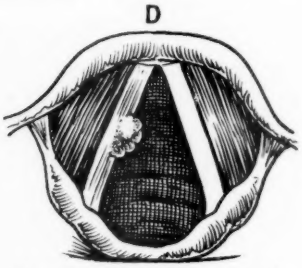
(D) A man aged 66. Warty growth of the middle-third of the right vocal cord. Hoarse two months. Growth removed by laryngofissure, December, 1923. No recurrence. Patient alive and well.

Section: Papilloma becoming malignant.

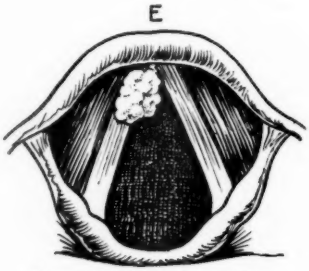
(**E**) A snow-white warty growth of the anterior third of the right vocal cord in a man aged 64. Hoarse twelve months.

Section after laryngofissure: Papilloma becoming malignant.

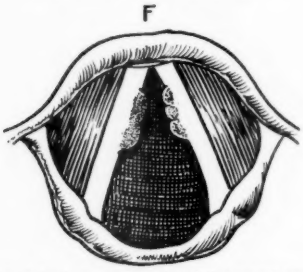
This is a type of case in which it is difficult to obtain a satisfactory pre-operative diagnostic specimen for microscopy. The piece of tissue removed, owing to the hardness of the growth, does not go deep enough for diagnosis. The same is true of a flat deep growth of a vocal cord.



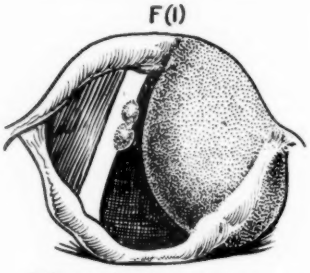
A papilloma becoming malignant.



A snow-white warty growth.



Symmetrical granulomata of the vocal cords.



A deep-seated adenocarcinoma. (Same larynx as in F.)

(**F**) Section of a deep-seated carcinoma from a woman, aged 47. First seen with symmetrical granulomata of the middle thirds of the vocal cords. Tuberculosis and syphilis excluded. Pathology and diagnosis obscure. (See fig. F.)

Condition in spite of treatment remained unchanged for eight years; then a smooth, solid tumour of the left ventricular band and the arytæno-epiglottidean fold appeared. (See fig. F (1).)

The tumour was removed by hemilaryngectomy and found to be an adeno-carcinoma.

The patient died fifteen months later from a recurrence of the growth in the neck.

Mr. Davis said that it was not claimed that these specimens showed precancerous conditions; only Specimen D might be called precancerous.

Specimen F was shown to illustrate a type of clinical case in which a deep-seated adenocarcinoma, probably commencing in the mucous glands and deeper structures of the larynx, resembled perichondritis. These growths frequently softened and became necrotic, as happened in this case which was thought before operation to be a case of perichondritis. The mucous membrane of the larynx was intact and the growth did not burst through the mucous membrane.

He had seen five cases of this type of deep growth, the diagnosis of which was difficult because the laryngeal mucosa appeared to be normal.

The symmetrical granulomata probably had no connection with the deep-seated carcinoma which developed seven or eight years later.

Specimen E was a papillomatous growth which was not very malignant. There was no recurrence in this case for thirteen months; the patient was then lost sight of and could not be traced. It would be useful to know whether such cases were malignant and if recurrence took place.

[Mr. D. F. A. Neilson here showed a coloured drawing of a case similar to case E. He had removed the papillomatous growth by laryngofissure a few months ago.]

Mr. Herbert Tilley said that his views on the subject were rather indefinite because he had often seen unilateral lesions which appeared to be benign, and yet a long clinical experience prompted the suspicion that they were probably early instances of carcinoma. He was accustomed to teach students that, in such doubtful cases, the diagnosis would generally lie between tuberculosis, syphilis, or malignant disease; if the first two could be excluded, it would be wise to act on supposition of the third.

It was sometimes argued that because a certain definite symptom, e.g., hoarseness, had been present for two or three years, it was unlikely that the lesion could be of a malignant nature. But he had seen cases of obvious carcinoma—and quoted two examples—which had long histories of loss of voice, and the appearance at operation, as well as microscopic sections of the growths removed, amply confirmed the diagnosis of cancer. Were the earlier phases in such cases precancerous? In Mr. Neilson's case—which he (the speaker) had seen—the microscopic sections did not show the usual features of a squamous-celled carcinoma. Nevertheless, clinical experience would probably be unanimous that such a condition would—sooner rather than later—undergo malignant transformation, and that the best treatment had been accorded to the patient if the laryngeal lesion were regarded as of a "precancerous" nature and operated on.

Mr. Harold Barwell said that, from the clinical standpoint, he thought there was no such thing as a precancerous condition of the larynx. Sir StClair Thomson had said that, in the majority of cases of cancer of the vocal cord which he had seen, the larynx had apparently previously been perfectly healthy. Mr. Colledge had shown a case in which cancer was engrafted on a scar in the larynx, but that was a case of exceptional rarity. Mr. Davis had shown a case which was reported as papilloma becoming malignant, but it would be as suitable to call it a case of cancer with a papillary excrescence imitating, in its early stages, an innocent growth. If one could see the base of it one would probably find that it was cancer from the beginning. We had all seen, and watched for years, cases of chronic laryngitis and of pachydermia. How many of them had become malignant?

There could be no doubt that irritation was a cause of cancer, in the larynx as elsewhere, but in the majority of cases a chronically irritated larynx did not become cancerous, so there was, no doubt, a further unknown factor. Probably some constitutional factor was of importance, and this was shown occasionally by cases in which the successful removal of a cancer was followed by a fresh primary cancer in another part of the body.

Therefore he considered that, from the clinical point of view, the Section was discussing what was non-existent.

Dr. J. A. Gibb said that a few years ago he had asked himself the question: Why should certain cells, under mutation, suddenly take on a rapid mitosis? A surgical colleague supplied him with a small scirrhous cancer of the breast. With the collaboration of an analytical chemist he sought for lecithin lipoid from the cells. From a small portion of the growth $\frac{1}{4}$ gr. of pure lecithin lipoid was extracted. Lecithin lipoid was found in the normal cell as a mere trace; it was necessary for the life and movement of the cell. It was present in certain glands such as

the suprarenal, thyroid, ovary, and pituitary, and its presence was necessary for the performance of the normal functions of those glands.

It had occurred to him that as lecithin lipoid was present in the cells of new growth, those cells would be hypersensitive to any form of irritation and would take on abnormal change in the form of growth. An examination of the cells of a sarcoma showed that they yielded a higher percentage of lecithin than did those of cancer, and a wart showed a still higher percentage.

It had further occurred to him that the most important metabolic gland was the suprarenal, and that as the active principle in this case was lecithin lipoid, the important factor in these cases of cancer which had a lowered resistance was some toxic effect on the suprarenal gland whose consequent lack of function might result in an excessive formation and deposit of lecithin lipoid in the cells, thus making them more sensitive to irritation. Mr. Colledge had mentioned that hyperglycæmia was found in cancer cases, and that bore out his (the speaker's) view with regard to the suprarenal gland. The chemist had prepared for him some lecithin lipoid, extracted from the cancer, in pure olive oil in suitable doses, in ampoules.

He, Dr. Gibb, had performed diathermy for cancer of the tongue, and the condition remaining had been foul and septic; half of the tongue had been removed. He had injected the patient with the lecithin lipoid taken from the carcinoma of the breast, and afterwards the tongue condition improved amazingly, the sepsis cleared rapidly and the patient had left hospital with a smooth clean scar.

The chemist had since been extracting lecithin lipoid from eggs, and this had been used with benefit.

He (the speaker) suggested that when a cancer was removed the adjacent cells should be examined for lecithin lipoid as that might be a guide as to the possibility of recurrence. Moreover, it might be taken as a suggestion of a precancerous stage.

Mr. Musgrave Woodman said that there were two points to be considered, one pathological, the other clinical. One of the sections exhibited showed an epithelioma which did not break through into the deeper layer, but there was a collection of round-celled iufiltration immediately below the unbroken processes. He asked how that could possibly be distinguished from chronic irritation. From the clinical side, one heard the expression "precancerous condition," but did that exist? It was known that in chronic interstitial glossitis, irritation went on a long time before epithelioma developed. Many cases of growth of the larynx started *ab initio* as a growth, without previous irritation. Therefore, by the term "precancerous" he suggested that what was meant was a chronic irritation, which merged into a growth. It was not a common occurrence.

CASES.

Papillomatous Condition of Vocal Cord. Case for Diagnosis.—C. A. SCOTT RIDOUT, M.S.

E. M., married woman, aged 47, first seen July 9, 1930, complaining of "husky throat" for about a year; much worse during last few weeks. On examination: Right vocal cord thickened, granular, moved well. Physician's report: "*Nil* in chest." Wassermann reaction, negative.

August 27.—Papillomatous appearance of right vocal cord very marked; portion removed with forceps.

Pathological Report.—Section does not show any evidence of a malignant tumour. (Section shown.)

Further progress: Apparently improved, but (October 8) right vocal cord is still distinctly thickened and papillomatous in appearance.

Dicussion.—Sir STCLAIR THOMSON said that pathologists were not infallible. If this were his own case he would suggest taking another specimen, deeply, and even then, if that were negative, he would have a laryngofissure carried out.

Mr. TILLEY said he would advise laryngofissure without hesitation.

Sir JAMES DUNDAS-GRANT said that there was a tendency to the formation of a cup in the anterior part of the growth, which, in his opinion, was an epithelioma.

Mr. RIDOUT (in reply) said he was in favour of removing the cord, and if the patient would allow it he would do so.

Swelling in Left Pyriform Fossa. Case for Diagnosis. — LESLIE POWELL, M.B.

F. G., female, aged 49, complains of difficulty in swallowing during last five months. No vomiting. Always thin, but recently some wasting.

Swelling of left half of larynx, not involving vocal cord. Cord sometimes fixed but has been seen to move. Swelling varies in size and some pus comes from left pyriform fossa. Speech normal; no pain.

Discussion.—Sir JAMES DUNDAS-GRANT said that the disease had apparently extended to the posterior wall of the pharynx.

The PRESIDENT said that the consensus of opinion was strongly in favour of this being epithelioma.

Dr. LESLIE POWELL (in reply) said that when he saw the case and arranged to send it up, no ulceration could be seen. Pus had escaped, and the swelling had varied in size; he had wondered whether it was a tuberculous abscess. The vocal cord was normal and was moving fairly freely.

Dr. JOBSON HORNE said he did not regard the condition as malignant; it seemed to be suppurative.

Specimen of Larynx with Pachydermia and Subglottic Epithelioma. —V. E. NEGUS, M.S.

The patient was an old actor, aged 80, with a history of hoarseness for some years. He had been examined by Mr. Harmer in 1923, when the larynx was normal.

Examined on December 25, 1929, because of severe dyspnœa and bronchitis; marked pachydermia, involving both vocal cords, was seen and a large subglottic swelling, apparently of malignant nature, was present.

Tracheotomy was performed four days later; the trachea had to be opened hurriedly, high up through the growth, but, after admission of air, a cannula was inserted lower down a few minutes later.

The patient died, January 1, 1930, from pneumonia. Post-mortem examination showed the presence of an epithelioma separated by a definite interval from the areas of keratosis on the vocal cords.

Specimen of Tongue, Pharynx and Larynx, showing complete disappearance of an extensive Carcinoma after the use of Radium.—HAROLD KISCH, F.R.C.S.

Patient, male, aged 66, attended hospital on December 30, 1929, complaining of complete disability to swallow solid or liquid. There was a history of increasing trouble during the last four months. On examination, the back of the tongue, the right side of the pharynx, and the larynx were found to be involved in an extensive ulcerating growth. Patient was admitted to hospital and a feeding tube was passed into the stomach. Portions of the growth were removed for examination and proved to be carcinoma. All the septic teeth were removed, and on January 9, 1930, radium needles were inserted into the tongue and upper part of the pharyngeal portion of the growth. The dose given was 1,320 mg.-hours, the needles being 1 mg. each. By January 19, the patient was able to swallow comfortably and the growth on the tongue had disappeared. Growth could now be seen occupying the right pyriform fossa and that side of the larynx was fixed.

February 12, 1930.—The preliminary stages of a lateral pharyngotomy were performed, but the pharynx was not opened. Radium needles were inserted, and a total dose of 1,848 mg.-hours given. Patient was discharged March 6, 1930, apparently quite well and swallowing perfectly.

He was seen again October 6, 1930, feeling ill, and having an enlarged gland in the neck on the right side. He was admitted for treatment of the gland, but was found to have broncho-pneumonia, from which he died on October 10, 1930.

Sections of the gland are being prepared. Sections of the original growth are shown, together with a section of a papilloma, with an implantation carcinoma, removed from the left tonsil.

FURTHER REPORT OF CASES PREVIOUSLY SHOWN.

Carcinoma of Larynx treated with Radon Needles.—W. STEWART, M.B.

A.M., male, aged 38. Shown previously in June, 1929.[1] The growth was then considered to be carcinoma of the left vocal cord. The cord was fixed.

July 17, 1929. Six 2 m.c. radon-needles, 0·3 mm. platinum screen applied through a window resection of left thyroid ala. Tracheotomy at end of operation. Radon needles removed on eighth day. Profuse purulent discharge from wound. Tracheotomy tube kept in two weeks. No biopsy was made.

The growth rapidly disappeared. There has so far been no sign of recurrence. The left cord moves freely. There is a moderately strong, somewhat husky voice.

Laryngeal Growth.[2]—L. GRAHAM BROWN, F.R.C.S.

P.S., male, aged 52, shown a year ago at a meeting of this Section. Consensus of opinion was that it was a case of chronic hypertrophic laryngitis.

In the year's interval there has been an obvious increase in the amount of hypertrophied tissue, in spite of medical treatment with mercury and potassium iodide.

A section of the tissue examined a year ago showed squamous epithelial cells in which the nuclei varied in size and shape, a few mitoses being present.

Is this a precancerous condition?

Discussion.—Mr. E. D. D. DAVIS (in the absence of Mr. GRAHAM BROWN) said that the Wassermann reaction was negative in this case, and no tuberculosis was present, as far as could be ascertained. There was no doubt that the growth was increasing. It had been thought to be pachydermia, but part of the section was papillomatous.

Sir STCLAIR THOMSON said that when this case was shown before, some Members had thought that the condition was malignant, but he (Sir StClair) had suggested that it was a form of hypertrophic laryngitis, and now, after a year, he still thought so. He could not think that malignant disease would spread all round the endolarynx, in the posterior two-thirds, without causing more distress than this patient suffered, or a deeper invasion of the cartilage. His only suggestion now was that a further biopsy should be made, because of the possibility of the case having become tuberculous.

Mr. HERBERT TILLEY said he would be surprised if a further section did not suggest malignancy: he felt convinced that that was the nature of the growth.

Epithelioma of the Vocal Cord treated with Radium.[3]—HAROLD KISCH, F.R.C.S.

Patient, aged 62, was shown at the November meeting, 1929. There is no recurrence of the growth. The dose was 600 mg.-hours.

1 *Proceedings*, 1929, xxii, 1559 (Sect. Laryng. 77). "Ulceration and fixation of left vocal cord."
2 *Proceedings*, 1930, xxiii, 515 (Sect. Laryng. 17).
3 *Proceedings*, 1930, xxiii, 375 (Sect Laryng. 7).

Section of Neurology.

CASES SHOWN AT THE MEETING HELD AT THE NATIONAL HOSPITAL, QUEEN SQUARE, LONDON, THURSDAY, DECEMBER 11, 1930.

Von Recklinghausen's Disease with Weakness and Ataxia in the Limbs, Spinal Curvature and Slight Acromegaly.—J. PURDON MARTIN, M.D.

W. E. P., male, aged 33. "Raised spots" have been present on his body as long as he can remember; one on right forehead appeared in boyhood and numerous "freckles" on trunk also appeared in boyhood, after scarlet fever. Curvature of spine was noticed when he was aged about 14. About five years ago began to experience difficulty in picking up small objects; also became unsteady in walking.

Over the trunk are numerous typical neuro-fibromata and "café-au-lait" patches. Larger subcutaneous tumour on right arm at lower border of deltoid.

No thickenings of nerve trunks in limbs have been found.

Sense of position is defective in both arms and in toes of both feet. Stereognosis greatly impaired in both hands. Tendon-jerks exaggerated; the plantar reflexes extensor; gait slightly ataxic. Superficial sensation everywhere normal.

Abnormality of the left optic disc (opaque nerve fibres).

Marked kypho-scoliosis. Bones of limbs show no deformity.

Features of face are "coarse" compared with the condition shown in a photograph of patient taken at age of 22, and hands are broad.

The patient's brother has several neuro-fibromata on the face.

Intracranial Calcified Mass.—J. PURDON MARTIN, M.D.

Patient, female, aged 18, has complete paralysis of left oculo-motor nerve and right hemianopia and atrophy of right optic disc. In addition she has bilateral hemiparesis, with typical reflex changes: left side of body is more affected than right. Stereoscopic skiagrams show large calcified mass lying chiefly to left of middle line, approximately in position of medial surface of temporal lobe; portion of this mass crosses middle line behind pituitary body. No signs or symptoms of any disturbance of pituitary function. (Suggested diagnosis: Calcification in large, supra-pituitary tumour.)

Bilateral Hemiplegia and Bilateral Optic Atrophy; Sudden Onset of Paralysis and Blindness.—J. PURDON MARTIN, M.D.

Patient, female, aged about 45. In March, 1928, suddenly became blind and immediately afterwards became unconscious (? convulsion). Does not know how long she remained unconscious. When she recovered consciousness she was still blind and was unable to move any of her limbs. During next few months became able to distinguish light, and to see large moving objects, and considerable power returned in the left arm.

Present condition.—Mentally, "slightly simple." Both optic discs atrophic; a light or a large moving object is perceived in nasal half of each visual field. Ocular movements normal. Appreciation of smell, auditory perception, and speech, all normal. Severe right hemiplegia, with contracture in right hand, and very severe impairment of all forms of sensation over right half of body. Left arm and leg are paretic, the leg being the more affected. Hair has receded from the forehead and anterior part of temples.

Cerebrospinal fluid normal. Skiagrams show nothing definitely abnormal.

Localized Fat Atrophy with Associated Wasting of the Underlying Muscles.—MACDONALD CRITCHLEY, M.D.

Patient, female, aged 38, a dancer, three months ago accidentally noticed that there was some wasting in left upper arm. About four weeks later became aware that the arm was weak, especially in movements at shoulder-joint. One month ago similar wasting seen in left thigh, and she found difficulty in supporting herself on that leg alone. Within the past two weeks the right upper arm has appeared to become affected in same way.

On examination, a bilateral and symmetrical atrophy of subcutaneous fat is noticeable in patches, especially in upper arm, below insertion of deltoid, and in outer aspect of thigh. The affection is much more obvious in the left limbs. Associated with the loss of fat there is some diminution in the bulk of the underlying muscles with some impairment in their power. No alteration in sensation or reflexes has been discoverable.

No abnormal pigmentation: skin everywhere normal in consistency and not indurated. No abnormal hardness to be palpated in muscles or subcutaneous tissues.

Family history: *Nil ad rem.*

Previous health uneventful, except for arthritis of left knee in 1922. for which patient was treated with vaccine.

Vertical Nystagmus.—T. R. HILL, M.D.

R. L., male, aged 51. Under the care of Dr. C. Worster-Drought. Slight right-sided ptosis since 1916. Six years ago walking gradually became impaired owing to tendency to drag right leg. Some slurring of speech developed three years ago.

Physical examination.—Pupils equal and react normally; fundi normal; on lateral deviation of eyes, coarse and slow vertical nystagmus is observed; not seen on upward or downward movements of eyeballs. Definite slurring of speech. Other cranial nerves normal. Sensation intact; deep reflexes generally brisk, but equal on the two sides; abdominal reflexes present and equal; plantar reflexes indefinite but mainly flexor. Slight intention tremor of both hands and some ataxia of lower limbs. Other systems normal. Wassermann reaction negative. X-ray of skull negative.

This case is shown partly for the interest of the vertical nystagmus, but chiefly because of the difficulty in diagnosing the actual disease-process.

Disseminated sclerosis is regarded as the most likely diagnosis, but the speech is by no means typical and no fluctuations have characterized the course of the patient's illness which has been slowly progressive. Syphilitic mesencephalitis was considered, but the normal pupillary reactions, as well as a negative blood Wassermann reaction, are against this. The signs and symptoms appear too selective to be due to a vascular lesion; also, the condition is progressive. Very tentatively the suggestion is made that the condition may be an atypical form of heredito-familial ataxia. All signs would thus be explained.

Recently the patient had a "fit," with no loss of consciousness. During this, his back muscles went in a tonic-spasm and remained so for some hours, producing partial opisthotonos. As the patient probably has a mesencephalic lesion, it is possible that this was a "tonic-fit"—a transient attack of incomplete decerebral rigidity.

Syphilitic Amyotrophy.—C. H. FOUCHÉ, M.B.

C. H., male, aged 37, noticed diplopia two and a half years ago, which at first was corrected by glasses but has steadily become worse.

One year ago had sore throat which did not clear up with ordinary treatment, and left behind dysphagia with nasal regurgitation of fluids and alteration in voice, which has become nasal and thick in character. General wasting and atrophy of all the skeletal muscles during past year.

Visual acuity normal; fields full to rough tests; discs pale and clearly defined. Pupils large, equal, central and circular; fixed to light and on accommodation. Extreme bilateral ptosis, right greater than left.

External ocular movements limited; no lateral movement and only slight range on looking up or down. When the eyelids are passively elevated there is diplopia, which the patient has ingeniously overcome by the judicious application of a piece of adhesive plaster extending from the right side of the forehead to the right upper lid.

Weakness and wasting of all the muscles of mastication, giving face a cadaveric appearance and causing dropping of lower jaw. Weakness of left lower face and complete paralysis of frontalis; he can neither frown nor wrinkle his forehead.

Hearing normal. Palate does not move on phonation; curtain movement of post-pharyngeal wall to right. Sternomastoids and trapezii, normal. Tongue protruded to left and shows certain amount of fibrillary twitching. Sensory system normal. Generalized wasting of muscles, although power at all joints is fair.

Deep reflexes all absent. Sphincters normal. Wassermann reaction strongly positive in blood. Cerebrospinal fluid: cells 10 per c.mm.; total protein, 0·08%; Lange, negative. Wassermann reaction negative.

Cataplexy.—C. H. FOUCHÉ, M.B.

A. B., male, aged 23, was quite well until four years ago. Whilst playing tennis he noticed that after making a particularly good stroke he became absolutely limp and could not make the return shot. He felt that he had to keep perfectly still for fear of falling. The attacks lasted from one to two seconds, the patient being quite aware of everything going on around him. On two occasions he has actually fallen, "just flopped down."

These attacks are also precipitated by hearty laughter and when he becomes angry. Since this last summer, he would on occasion waken at night with feeling of limpness and "twitching of jaw." On one occasion there was stiffness of muscles of back, and, on two occasions, of right side of face. Feels weak when on his legs, and tires easily.

For past six to nine months has had feeling of strain in right eye; no diplopia, but a feeling as if eye is turning outwards.

No polyuria. Had concussion nine years ago; made a complete recovery. No history of epilepsy in family, or of convulsions in patient's own childhood.

Physical examination negative, except for right-sided facial asymmetry and drooping of right shoulder.

Cerebellar Lesion ? Tumour.—T. R. HILL, M.D.

D.W., a girl aged 12. Onset of illness about a year ago with headaches and occasional vomiting. Headaches continued most days and vomiting about twice a week up till September last. Headache localized particularly to back of head.

Physical examination.—Bilateral nystagmus, chiefly to right; bilateral papillœdema of about 1·5 diopters; other cranial nerves normal; slight dysdiadokokinesia of right arm; Rombergism with tendency to deviate to right on walking. Blood Wassermann reaction negative; cerebrospinal fluid normal.

Since September, symptoms and signs have improved, with the exception of nystagmus and papillœdema which remain the same.

Palatal Nystagmus.—A. GILPIN, M.B. (introduced by Dr. MACDONALD CRITCHLEY).

Male, aged 67, complains of weakness of left arm and twitching of corner of mouth. In March, 1930, had attack of giddiness, nausea, and headache; no loss of consciousness but was confined to bed. In April, 1930, present symptoms began to be noticed.

Past history.—Rheumatic fever and syphilis 20 years ago. Diplopia 20 years ago. Gradual oncoming blindness in right eye for 15 years; completely blind in this eye for 2 years.

On examination.—Slight bilateral lid retraction, right greater than left. Optic atrophy, right eye. Pupils: right greater than left. Left reacts to light with consensual reaction in right eye. Fine continual vertical nystagmus of right eye, especially marked on right lateral and upward ocular deviation. Slight weakness of left side of face. Jaw moves symmetrically. Tongue protruded straight.

Facial, palatal, pharyngeal, laryngeal nystagmus.—There is a regular uniform constant movement of the left lower lip and a regular upward movement of the soft

palate, rather more marked on the left side, so that the palate moves upward and slightly to the left. A similar movement is present in the oro-pharyngeal muscles, the vocal cords and aryepiglottic folds; it is bilateral and synchronous with the facial and palatal movements. On voluntary movements of the affected muscles the involuntary movements are damped down in amplitude. Abduction of the vocal cords is executed well.

There is a slight increase of tone in left arm and leg. All movements are weaker in left arm and leg compared with right. Fine manipulative movements impossible in left hand and there is a falling away of left outstretched arm. Finger-nose and finger-finger tests show a cerebellar type of dysfunction in the left arm; similar but milder condition is present in left leg. All tendon-jerks are brisk. Left arm greater than right arm. Abdominal jerks present. Double flexor plantar response. No sensory loss.

Gait.—Cannot walk unaided. Tendency to fall to left with gross unsteadiness.

Patient complains of his breathing—feels "short of breath," especially at certain times, when breath "catches." There is an objective noisiness and irregular irregularity of rhythm and amplitude of the respirations.

X-ray (screening). Diaphragm.—Both cupolæ show a tremor-like movement of about the same frequency as the palatal tremor.

Marked salivation.

Some difficulty in swallowing.

Definite tendency to spontaneous laughter and crying.

Heart.—Enlarged slightly. Apical systolic murmur. *Blood-pressure.*—Systolic 265. Diastolic 160.

Urine.—Trace of albumin. *Blood Wassermann.*—Positive. *Cerebrospinal fluid.*—Protein slightly increased. Wassermann negative.

Paget's Disease of Spine, causing Compression of Cord.—DENIS BRINTON, B.M.

W. B., male, aged 58, admitted to National Hospital in January, 1930, under Dr. Gordon Holmes, complaining of weakness and stiffness of lower limbs and hesitation of micturition, both of six months' duration.

November, 1927, operation for cholecystitis, following some years of recurrent abdominal pain in right upper quadrant: some immediate relief, but further pain began very soon lower down and, with it, a sense of constriction from a little above the umbilicus downwards: these symptoms remained constant till time of admission. With sudden changes of position has occasionally had a stabbing sensation just below right lower costal margin.

Twelve months before admission slight aching and stretching pains in both knees brought on by any sudden movement; after six months, pains began to extend upwards to thighs and eventually mingled with abdominal pain.

On examination (January 6, 1930).—Motor Function.—*Trunk*: No contraction of intercostal muscles from the 6th downwards. Feeble, but symmetrical, contraction of abdominal muscles on attempting to sit up. *Lower limbs*: Bilateral weakness of all movements, especially dorsiflexion of feet and extension of knees. Increase of tone in extensors of hips and knees, and in plantar-flexors. *Reflexes*: abdominals absent; plantars extensor. Knee- and ankle-jerks brisk. No clonus.

Sensory function: Deep—but not complete—impairment to pin-prick and cotton-wool to level of 9th, with zone of diminished appreciation up to 5th dorsal segment. Heat and cold sensibility greatly impaired below 6th dorsal segment. Vibration sense lost below 7th dorsal spine, and over skin, below level of 6th rib anteriorly. Sense of position fairly accurate in toes.

Spine.—Tenderness on percussion of 5th, 6th and 7th dorsal spines. Skiagrams show advanced spondylitic changes.

Blood Wassermann reaction negative.

Skiagram.—(Skull, femora and upper tibiæ). Appearances suggest early Paget's disease of skull.

January 24, 1930.—Laminectomy: (2nd to 6th dorsal) by Sir Percy Sargent. Canal found to be narrowed by soft, cheesy, much thickened bone. Theca not opened.

Portion of lamina removed at operation reported to be histologically typical of Paget's disease. (Dr. Greenfield.)

Patient made an uninterrupted gradual recovery.

Pneumencephaly following Fracture of Skull.—DENIS BRINTON, B.M. R. W., male, aged 24, admitted to National Hospital under Dr. Gordon Holmes on five occasions between February, 1927, and October, 1929.

November, 1926: Fractured base of skull in motor-bicycle accident: in bed 3½ weeks.

January, 1927: Sudden attack of stiffness in right hand, with subsequent awkwardness in use of arm: weakness of right leg: diplopia.

(First admission) 2 D. of swelling R.O.D., diplopia, slight right hemiparesis (February). First attack of aphasia (April). First right-sided epileptic attack (July). Skiagram of skull. Large sharply-defined translucent area in left parietal region over upper Rolandic area, suggesting possibility of intracranial encysted collection of gas (October 3).

October 28, 1927: *Operation* (Sir Percy Sargent).—Smooth-walled intracerebral cavity found: posterior border ¼ in. anterior to left Rolandic fissure: yellowish fluid evacuated: no definite evidence of gas.

October, 1929: Examination on last admission showed: Slight nominal aphasia. Fundi. Hyperæmic discs and full veins: no swelling. Left eye slightly further forward than right. Diplopia. Only disability of motor function, cannot stand on tip-toe so long on right foot as on left. Sensory function and reflexes normal. Skiagram of skull: no evidence of intracranial gas. Had noticed a constant clear watery discharge from the left nostril from a few days after operation (28/10/27) up to last summer: none since.

Last seen: November, 1930. Occasional attacks of aphasia and of convulsions (usually with loss of consciousness) have recurred since these were first noticed (1927) up to the present time.

Two Brothers affected with Dystrophia Myotonica.—J. ST. C. ELKINGTON, M.B. (introduced by Dr. CARMICHAEL).

Family history.—Father suffers from difficulty in relaxing his grasp, and is losing flesh. His condition has never been sufficient to prevent his working. He remembers that when in the Army, at the age of 18, he was unable to carry coal boxes, because "his hands would not grasp." He has a typically myopathic appearance. His only brother, older than himself, is believed to be normal. His mother suffered from cataract at 40, but there is no other significant fact in his family history.

Mother alive and well. No history of myotonia, muscular wasting, or cataract in her family.

Their offspring, four boys and one girl, are as follows:—

> John M., aged 21, cannot relax his grasp. Is said to be very thin, keeps his mouth open and looks vacant. Is unable to work. Is single, and has never taken any interest in the opposite sex; William M., aged 19. Believed to be quite well; Rosie M., aged 17, also believed to be quite well, Albert M., aged 15 (Case I); Eric M., aged 10 (Case II).

Case I.—Albert M. Complaint: inability to relax grasp; indefinite duration (more than five years).

Past history.—Negative.

He first noticed that when he grasped a pen he was unable to let it go. This condition came on gradually and was always worse in cold weather. Power in hands is good. Legs are strong and do not let him down. He plays games and runs races, but only indifferently, and is backward at school. No trouble with eyesight. Never dribbles, but has never been able to whistle.

On examination.—Poorly developed for his age. Height 4 ft. 10 in. Nervous movement of head and shoulders. Myopathic facies, with broad forehead, tapering face, protuberant lips and slightly drooping eyelids. Facial movement limited during conversation; tendency to salivation. Head held forward as if too heavy for neck. Highly arched palate. Secondary sexual characters poorly developed for age; a few downy hairs on upper lip, pubic hair just erupting. Well-marked lumbar lordosis.

Cranial nerves.—Myopathic face; sad, transverse smile; unable to wrinkle forehead or to whistle. Tongue small and wrinkled, with myotonic reaction on percussion. Sternomastoids present and not noticeably wasted.

No other abnormality.

Motor system.—Upper extremities show general paucity of musculature; well-marked myotonia on voluntary contraction and upon percussion in flexors and, to a less extent, extensors of fingers. The trunk musculature is very dystrophic; ribs being unduly prominent. Is able to raise himself from ground without the use of his arms three times and then fails.

Legs normal except for slight wasting of internal vasti. Myotonic reaction is present upon percussion of anterior tibials and peronei on each side. Reflexes, normal. Sensation, normal.

Eyes.—No evidence of cataract (to clinical examination).

Genitalia, poorly developed for age. Other systems, normal.

Case II.—Eric M.

Complaint.—Inability to relax hand-grasp (for two years).

Past history.—Negative.

Trouble was first noticed in winter, when hands went cramped and would not relax after grasping a pen.

On examination.—Small delicate child with solemn expression and immobile face, devoid of any lines. Movement practically lacking from the forehead; shape of mouth is symmetrical, but movement is poor in range; able to whistle. Palate highly arched. Genitalia small for age. No secondary sexual characters present. Marked lumbar lordosis.

Cranial nerves normal except for facial musculature, and tongue, which is well-formed, but shows marked myotonic reaction to percussion.

Motor system.—Sternomastoids present, not appreciably wasted in comparison with muscles of the trunk.

Upper limbs generally of poor development; no one group of muscles being more affected than others. Well-marked myotonic reaction after voluntary contraction on percussion in forearm flexors and, to a less extent, in extensors; more marked left than right. Trunk shows marked wasting, with prominent ribs, and lordosis.

Legs noticeably well developed in comparison with rest of body.

Leg muscles show no abnormal reactions. Reflexes, normal. Sensation, normal.

Eyes.—No clinical evidence of opacity. Other systems normal.

Exophthalmos and Conjugate Ocular Palsies following Encephalitis Lethargica.—W. RUSSELL BRAIN, M.D.

J. E., male, labourer, aged 59. In June, 1927, began to suffer from headache, drowsiness, giddiness, diplopia and tremor of the right upper limb. Admitted to London Hospital, October, 1927. Was very drowsy, and euphoric when roused.

Fundi normal; slight right exophthalmos; pupils unequal, left larger than right, reacted to light; bilateral ptosis; ocular convergence completely lost; conjugate deviation upwards feeble; lateral and downward movement of eyes, good, but associated with nystagmus. Slight left hemiparesis, with left extensor plantar response. Gross intention tremor right upper limb. Cerebrospinal fluid, normal. Bradycardia.

Drowsiness increased at first, but, after two weeks, improvement began. Three months after admission to hospital no physical signs, except tremor of right upper limb. Returned to work. One year ago relapsed with slight drowsiness, headache, and diplopia. Since then there has been increasing prominence of eyes, which are painful.

Has had right otorrhœa many years ago, with residual deafness.

Present condition.—Fundi normal; exophthalmos, right more than left; pupils moderately contracted, react to light but not on accommodation; divergent squint; ocular convergence feeble; conjugate ocular deviation upwards lost; lateral deviation fair, abduction better than adduction, both eyes; downward movements good; ptosis of upper lids, especially right, but exaggerated retraction, especially left, on attempting to look up. Cranial nerves otherwise normal; slight tremor of right upper limb; muscle tone and tendon reflexes slightly greater on right side than left; plantars flexor; no sensory loss; gait normal; facial seborrhœa: hyperidrosis of hands and feet; increased sugar tolerance, with low renal threshold; weight stationary; pulse 72, blood-pressure 130/70; heart normal; no enlargement of thyroid; skiagrams of skull normal; cerebrospinal fluid, normal.

Progressive Muscular Atrophy; Atonic Atrophy without Fibrillation.—D. DENNY-BROWN, M.B.

E. H., a clerk aged 37 years, underwent operation on account of right torticollis at an early age, and has avoided rough sports ever since. No history of muscular weakness. In June 1930, noticed weakness in both arms. After a rest at home for a week during which both arms became stronger, again became weak and noticed slight weakness of both lower limbs. After a prolonged rest at seaside during which condition twice improved and then relapsed, noticed marked wasting of upper arms; late in August became very weak in both arms. Admitted to National Hospital, Queen Square, under Dr. J. Purdon Martin, September 2, 1930.

On admission.—Extreme weakness and marked wasting of biceps and triceps in both upper limbs; severe weakness of both deltoids and slight wasting of left deltoid. Contractions of both sternomastoids and both trapezii fairly easily overcome, but these muscles were not wasted. No other weakness or wasting could be demonstrated in either upper limb. Slight weakness in flexors and extensors of both hip-joints, and in dorsiflexors of both ankles, but no other weakness and no wasting in lower limbs. All musculature was flaccid, and, other than a coarse twitching once observed in right biceps, no fibrillation of any kind was seen during the period of his stay in hospital. Electrical reactions of affected muscles consistently normal; no reaction of degeneration. All tendon-jerks brisk on both sides, except ankle-jerks which are feeble. Abdominal reflexes present and brisk; plantar responses both flexor. No sensory changes.

He gradually became stronger under treatment and was discharged 10.10.30, with adequate but not quite full power of flexion and extension of elbows and abduction of upper limbs. No other weakness; wasting and reflex responses remained as on admission. After ten days at home he went back to work, but three days later a herpetic eruption developed on left side of abdomen; he was recovering from this when five days later he noticed some weakness in both arms. After another week this weakness became severe and both lower limbs became weak. After another week he was readmitted to the National Hospital under Dr. Martin 14.11.30.

He had at no time had any symptoms or signs suggesting weakness of extra-ocular or other cranial muscles.

He was now found to have thin, weak sternomastoids, slightly weak trapezii, with wasted lower segments, but fairly strong pectoral muscles, only slightly thinned. Latissimus serratus and rhomboid groups strong and not wasted; spinati weak and wasted on both sides; deltoids both extremely wasted, especially left, and both almost completely powerless. Triceps and biceps on both sides powerless and extremely wasted. Dorsiflexors of wrist, extensors of fingers and intrinsic muscles of hands now a little weak, and these muscles showed some wasting, especially on left side. There is symmetrical moderate weakness of trunk musculature. Extension and flexion of both knees and flexion of left hip very weak; slight general wasting of both quadriceps and hamstrings. Musculature still flaccid, and not until three days ago, when some flickering in left rhomboids was seen, was any fibrillation observed in any part. This has been absent since.

Sluggish ankle-jerks still present, but other tendon reflexes are absent. Both upper abdominal reflexes present. Plantar responses flexor on both sides. No sensory changes. No reaction of degeneration in affected muscles. Contractions become noticeably less after from 100 to 200 responses.

He has a smooth face, but strong facial musculature. He has almost complete frontal baldness. Fine nystagmus on extreme lateral deviation, but no strabismus or ptosis. Tongue, masseters and temporal muscles unchanged.

Sub-arachnoid Hæmorrhage with double Vitreous Hæmorrhages.—DOUGLAS N. BUCHANAN, M.B. (introduced by Dr. ADIE).

E. W., female, aged 41. Complaint: Blindness in both eyes, and severe headache since August 23, 1930; unconsciousness from August 18 to August 23, 1930. History of attacks of headache two or three times each week during period 1927 to 1930. Usually on waking in morning, wearing off by lunch time; the character of continual shooting pain arising in parietal region and extending down to the tip of the nose. Not more frequent on one side than on the other.

August 17, 1930. Sudden attack of severe occipital pain lasting ten minutes. Next day awoke with diffuse headache and that afternoon she suddenly fell unconscious. She regained consciousness five days later and discovered that she was quite blind. Has been told that during these five days she was paralysed down the left side of her body.

Headache has persisted from August 23 until admission.

On examination.—Light perceived by both eyes; form and movement unappreciated with right eye. Movement appreciated with left eye. Both eyes show vitreous hæmorrhage; fundi completely obscured. Both pupils dilated, left wider than the right; both react to light direct and consensual; no limitation of ocular movement in any direction.

Slight right facial weakness. Deep reflexes present and brisk symmetrically. Plantar responses flexor.

Area of cardiac dullness enlarged. Systolic and diastolic murmur at aortic area transmitted down sternum. Systolic murmur audible at mitral area. Blood-pressure 90/60.

No abnormality detected in any other system.

Section for the Study of Disease in Children.

[*November* 28, 1930.]

Report on Two Cases of Septicæmia following Tonsillectomy.

By W. R. F. Collis, M.D.

(*With permission from the Medical and Surgical Staff, Hospital for Sick Children, Great Ormond Street.*)

I.—Girl, aged 4 years and 10 months. Recommended for tonsillectomy on account of snoring, frequent colds, complaints of earache and enlarged cervical glands.

Operation.—Tonsillectomy by enucleation method, October 23, 1930. The throat did not look red and the tonsillar glands were no longer enlarged. A small peritonsillar abscess was found. Nothing else unusual was noticed at operation. The following day a high, swinging temperature commenced and the child died, with all the symptoms of septicæmia, on October 24.

At autopsy the liver showed fatty degeneration and the spleen was soft, the Malpighian corpuscles standing out prominently on section. A hæmolytic streptococcus was isolated from the heart's blood and Dr. Griffith of the Ministry of Health kindly typed and classified it as type 1 scarlet fever streptococcus.

II.—Girl, aged 7 years and 4 months. Recommended for tonsillectomy on account of ear discharge, sore throats, frequent colds, and snoring at nights.

Operation.—Tonsillectomy the same day as in Case I (October 22, 1930). Tonsils were noticed at operation to be enlarged and to show inflamed follicles, and the tonsillar glands were enlarged. The operation was performed without incident, and the following day all the symptoms of septicæmia developed, with high swinging temperature, rigor and blood and albumin in the urine, and the child died on October 24.

Autopsy showed a condition exactly akin to that in Case I, though cultures were unsatisfactory, due possibly to the necessary delay in performing the autopsy. Subsequently we heard from the Medical Officer of Health for Barnes that the father and sister of this patient had developed scarlet fever at the same time. Swabs were obtained from their throats and the presence of the same type of scarlet fever streptococcus as that found in the heart's blood in Case I was demonstrated.

The children were not operated upon in succession, but lay next each other in the recovery room after operation. It seems probable that the patient in Case II had an early active scarlet fever throat at the time of operation and conveyed the infection to the patient in Case I while in the recovery room. The raw areas after operation would account for the rapid admission of the organism into the blood stream, since organisms can gain access to the blood-stream from a raw surface in less than five minutes.

It is possible that the small peritonsillar abscess in Case I was infected with the organism, and—that its opening at operation led to the septicæmia in this case. It would, however, be much more unlikely for two cases to be infected with the same identical organism (e.g., type 1 hæmolytic scarlet fever streptococcus) independently on the same day, and to die within forty-eight hours with identical clinical symptoms, than that one should convey the infection to the other.

Now these two cases were operated upon in the Tonsil Clinic at Great Ormond Street, where the surgical conditions are as near perfect as possible. Every case is thoroughly overhauled, temperature taken and urine examined before operation. They are operated upon under deep ether anæsthesia by a skilled surgeon and every tonsil is enucleated. After operation all cases are admitted to hospital.

If, then, such a tragedy as this can occur in such conditions, it makes one wonder if our attitude in recommending such large numbers of children for tonsillectomy is justified, especially since it is a matter of common knowledge that many operations are daily being performed with far less careful precautions.

The patients in the cases just quoted were recommended for tonsillectomy merely on account of catarrh, and would now be alive and well if no operation had been performed.

I submit that our attitude towards this subject needs to be most seriously reconsidered.

[Drs. Feldman, Parkes Weber, E. W. Goodall and others took part in the discussion.]

CASES.

Schilder's Periaxial Encephalitis.— C. WORSTER-DROUGHT, M.D., and T. R. HILL, M.D.

F. H., male, aged 7 years.

History.—Normal until six months ago: (Previous illnesses: measles, pertussis, chicken-pox). Psychical abnormalities then developed gradually, child becoming spiteful, and laughing when corrected; then unduly sleepy and weak on his legs. One month later: frequency of micturition; great difficulty in walking; ankle-clonus and double extensor plantar response; failure of vision and hearing; bilateral ptosis. Condition has steadily progressed until the present time.

Present condition.—Unable to stand or walk; is blind, deaf and dumb; shows signs of fair intelligence when these sensory defects are penetrated, e.g., discriminates between individuals, articles of food, etc., and shows good memory.

Pupils moderately dilated, sluggish in reaction to light; double ptosis; complete blindness; fundi normal. Total deafness. Common sensation apparently normal. Tone, power, and co-ordination good in upper limbs. Abdominal reflexes absent. Legs possess some power, but are inco-ordinate and frequently show scissor spasm and spasmodic foot-drop. Knee-jerks exaggerated; plantar reflexes extensor. Incontinence. Cerebrospinal fluid: cells, 7 lymphocytes per c.mm.; no excess of protein; Wassermann and Lange reactions negative. Blood Wassermann reaction negative.

Commentary.—The case exhibits central defects of vision, hearing, and motor power, as well as psychical abnormalities. The onset of these symptoms occurred only six months ago and they are presumably due to simultaneous degeneration (demyelinization) in the white matter of the occipital, temporal, parietal and frontal lobes. The diagnosis, therefore, could scarcely be other than that of the subacute type of Schilder's periaxial encephalitis.

We are indebted to Dr. Borthwick, Medical Superintendent of the Northern Hospital, Winchmore Hill, for kindly allowing us to show the case.

Double Hemiplegia following Diphtheria.—C. WORSTER-DROUGHT, M.D., and T. R. HILL, M.D.

J. C., male, aged 13 years.

History.—Admitted to the Eastern Fever Hospital, September 9, 1929, with severe attack of diphtheria; membrane on soft palate as well as on tonsils. Signs of cardiac weakness for about ten days. Nineteen days after onset of illness

appeared semi-dazed and did not reply intelligently to questions. Paresis of right side of face and of right arm rapidly developed. Two days later, partial motor aphasia and right hemiplegia with right extensor plantar response were noted. On following day double extensor plantar response was observed. Slight improvement began, but twenty-five days after onset of diphtheria, a generalized epileptiform attack occurred, after which both legs were held in flexion and the patient became incontinent. The cerebrospinal fluid at this time was normal.

Present condition.—Unable to stand or walk. Legs usually extended and crossed by adductor spasm. At times pronounced flexor spasms occur. Right arm shows brisk tendon reflexes and frequent athetotic, automatic and associated movements. Some voluntary control in this limb and in the legs. Left arm normal as regards

Double hemiplegia following diphtheria. (Dr. Worster-Drought's case.)

tone and movement. Patient is of average intelligence and understands questions, but has complete motor aphasia. Facile laughing and crying frequently occur. A certain degree of "pseudobulbar paralysis"; mouth usually held open; tongue cannot be protruded; constant sialorrhœa and some difficulty in swallowing. Pupillary reactions and extra-ocular muscles normal. No facial weakness. Tendon reflexes: right arm reflexes brisker than left, knee-jerks brisk; bilateral spasmodic foot-drop. Plantar reflexes now flexor. Abdominal reflexes sluggish but equal. Marked hypertonia in legs. No definite sensory abnormality. Incontinence.

Commentary.—Hemiplegia as a complication of diphtheria is of rare occurrence. J. D. Rolleston, writing in 1925, states that barely 100 cases have been recorded since the first example was described by Sir William Gull in 1859. Rolleston, himself, met with only eight examples in 11,313 cases of diphtheria. Two cases

were shown to this Section during last Session. So far as we are aware, however, no case of bilateral cerebral involvement has been described. In all the recorded cases the diphtheritic infection was of a severe type and the complication usually developed within the first six weeks of illness.

The present case admits of three possible explanations: (1) That a bilateral cerebral embolism, or thrombosis, has occurred, involving the lenticulo-striate branches of each middle cerebral artery and leading to softening of both internal capsules and, later, of the basal ganglia. The left cerebral hemisphere was the first affected and the right a few days afterwards. (2) That the condition results from a true diphtheritic encephalitis. Encephalitis and encephalo-myelitis are now well known to be associated with other exanthemata, such as measles, but few, if any, possible examples of diphtheritic encephalitis have been described. (3) That an independent encephalitis has occurred somewhat comparable to the encephalo-myelitis following vaccination, and coincident with the severe diphtheria. Under these circumstances the diphtheria would play the part of the "activator" by lowering the patient's resistance and allowing the possible, but unidentified, virus of encephalo-myelitis to attack the patient.

In those cases of diphtheritic hemiplegia (unilateral) that have been examined post-mortem, embolism has usually been found to be the cause of the cerebral lesion. The first explanation, therefore, appears the most probable. The lesions are evidently deep and extensive as both pyramidal and extrapyramidal systems have been affected.

We are indebted to Dr. Pereira for kindly allowing us to make use of the notes taken at the Eastern Hospital, and to Dr. Borthwick, Medical Superintendent of the Northern Hospital, for permission to record the case.

Discussion.—Dr. J. B. ROLLESTON said that this was the first case which he had seen of double hemiplegia following diphtheria, though during twenty-five years he had seen twelve cases in which hemiplegia followed diphtheria. Was there any question in this case of ordinary diphtheritic paralysis? Because in a large proportion of these cases of hemiplegia ordinary diphtheritic polyneuritis was also present. Most authors agree that the hemiplegia was due to an embolic process, not to thrombosis; but several had suggested that it was due to an encephalitis, as could be seen from the paper published by Dynkin,[1] of St. Petersburg, in 1913. In 1916, he (Dr. Rolleston) [2] had shown a case of transient diphtheritic hemiplegia in which the hemiplegia, unlike most of the cases of hemiplegia following infectious diseases, lasted only twenty-four hours, and was probably due to more or less microscopic emboli. In the majority of the cases of post-diphtheritic hemiplegia which he had seen the patients had survived, but the hemiplegia had persisted. In fatal cases he had seen emboli in the kidney and spleen; emboli had also been found in the brain and elsewhere, e.g., in the popliteal artery, causing gangrene of the leg, as in a case he had reported to the Section.[3]

At least three cases of chorea having followed diphtheria were on record, namely, by Globus,[4] Critchley,[5] and Angarano[6] respectively.

Dr. E. W. GOODALL said that in these rare conditions after acute infections it did not follow that the two diseases were causally connected; it might be no more than a coincidence. He had seen chorea come on in patients who were convalescent from scarlet fever and diphtheria.

He agreed that the cause in these cases of hemiplegia was embolism, and, in diphtheria especially, there might be cardiac ante-mortem thrombosis. He did not remember to have seen a post-mortem examination on a patient who had had this form of paralysis after diphtheria.

1 *Jahrb. f. Kinderheilk.*, 1913, lxxviii, Erg.-Heft 267.
2 *Proceedings*, 1915-16, ix (Sect. Dis. in Child.), 53.
3 *Ibid.*, 1910-11, iv (Child. Sect.), 10.
4 *Zeitschr. f. d. ges. Neurol. u. Psych.*, 1923, lxxxv, 414.
5 *Brit. Journ. Child. Dis.*, 1924, xxi, 188.
6 *Pediatria*, 1927, xxxv, 725.

Progressive Muscular Atrophy of Spinal Origin.—W. G. WYLLIE, M.D.

Donald M., aged 2 years and 6 months. Born at full term; normal delivery. Sat up at age of 6 months; stood up at age of 10 months. One other child in the family, healthy.

When 12 months old patient lost power of standing; could crawl but was unable to get on to his feet. Weakness of limbs is proximal more than distal. Arms cannot be raised above head, although hand movements are fairly good. Movements at hip weaker than those at knee and ankle. Hands show a titubatory tremor, possibly due to muscular fibrillation which is not visible owing to fat covering limbs. Spinal muscles have become weak. On palpation, muscular wasting is appreciable in upper arm and thigh. Knee- and ankle-jerks absent; arm-jerks feeble. No sensory changes or sphincter disturbance. Cranial nerves and mental condition normal.

The muscular weakness is slowly progressive.

Hereditary Ectodermal Dysplasia.—JEAN SMITH, M.D.

A. B., male, aged 13 months. First brought by his mother because of his striking resemblance to an older brother shown at a meeting of this Section in January, 1929.[1] Chief characteristics: (fig. 1) peculiar facies; sparse fair hair; dry scurfy scalp; dilated scalp veins; thick everted lips: depressed nasal bridge; large projecting ears; absence

FIG. 1.—Alfred and Alan B., aged 6½ years and 12 months respectively. (Dr. Jean Smith's case of hereditary ectodermal dysplasia.)

of sweating; dental abnormalities (as shown in the skiagrams) and a tendency to attacks of high pyrexia unassociated with other constitutional disturbances. On the eleventh day after birth the temperature was 108° F., and persisted above normal for twenty-four hours, although the only explanation forthcoming was possible over-clothing. Skiagrams taken at the ages of 6 and 12 months respectively, show

[1] *Proceedings*, xxii, 1929, 619 (Sect. Dis. in Child., 54).

FIG. 2.—ALAN B., aged 11 months. Antero-posterior view of skull showing conical teeth in upper incisor position and absence of many other teeth.

Sabre tibia. (Dr. Schlesinger's case of syphilitic osteitis and periostitis.)

characteristic cone-shaped teeth in the upper incisor position, and absence of other teeth except two molars on either side of upper and lower jaws (fig. 2). No teeth have yet erupted. Teeth seen in skiagram can be represented by a dental formula which is apparently the same as that of his older brother. All other epidermal appendages appear to be normal.

Last year I could only trace fifteen cases of the anhydrotic type in the literature, whereas in a French-Canadian family group, most of whom live in Quebec, it has been possible to record no less than 119 cases in six generations.[2]

Syphilitic Osteitis and Periostitis: Sabre Tibiæ.—BERNARD SCHLESINGER, M.D.

D. W., a girl, aged 9.

Present history.—Aching of legs at night; loss of weight; general debility.

Past history.—Marasmus as a baby; snuffles at birth.

Family history.—Three other children alive and well. Four miscarriages.

On examination.—Marked enlargement of the tibiæ and fibulæ with some bowing. A suggestion of commencing Hutchinson's teeth. Wassermann reaction markedly positive.

In this case the fibula also is affected, which is unusual, the tibia being generally the bone involved. Under treatment the symptoms have abated and the sharp pains at night, which kept the child awake, have vanished. I was particularly impressed by her general good health despite the subacute inflammation of the bone, which points to a still active spirochætal infection. The case is shown as a variety of congenital syphilis relatively uncommon to-day. About twenty years ago this form of bone involvement was often seen, and when the lesion broke down it used not infrequently to be diagnosed as osteomyelitis.

This morning, curiously enough, I saw a family illustrating third generation congenital syphilis. The mother, who had brought up her syphilitic child for examination, had been operated upon for supposed osteo-myelitis fifteen years ago, at the age of 12, in Great Ormond Street Children's Hospital. That was before the days of the Wassermann test. The surgeon, however, found only gummatous tissue, and there was a discharging sinus which healed under treatment with mercury and iodide of potassium.

Discussion.—[Some speakers hinted at a doubt of the congenital character of this manifestation.]

Dr. H. STANNUS said: It may be of interest to recall the fact that sabre tibia is not an uncommon lesion in yaws, a disease due to treponema closely allied to *T. pallidum*. It is most commonly seen in persons above the age of five years. It is due to a framboesial osteitis. Framboesia is never inherited and the sabre tibiæ are always due to the acquired disease, a fact which perhaps might be allowed to argue against the similar condition in syphilis being necessarily a sign of the inherited disease.

Signs of heredo-syphilis are rarely seen among natives even in areas where the disease is widespread, and many of the facts observed in the study of syphilis among native races support the idea that the disease is acquired in early childhood—that, in fact, they "take syphilis just as they take measles," and that the syphilis seen among them is the acquired—not the inherited—disease.

[*The report of other cases shown at this Meeting will be published in the next issue of the* PROCEEDINGS *of the Section.*]

[2] Clouston, H. R., *Can. Med. Assoc. Journ.*, 1929, xxi, 18.

Section of Otology.

President—Mr. A. R. TWEEDIE, F.R.C.S.

[*November* 7, 1930.]

PRESIDENT'S ADDRESS.

The Eustachian Tube.

By A. R. TWEEDIE, F.R.C.S.

IT was difficult to decide on a subject for this address which should be at once commensurate with the occasion and the audience.

Out of a mere "side issue" of the head, in more senses than one, we have elaborated an auditory and vestibular apparatus, flinging, as the last word on the former, Part I of the Report of the Hearing Tests Committee to our Section to read—or rend—with determined threats of yet further parts, whilst the latter function has been separated into kinetic and static senses with their separate peripheral and central connections, and even more daring adventurers have explored the subtleties of the statocyst or sought solace in swim-bladders. Nothing, surely, has escaped attention.

With all these various considerations I felt some relief, on asking myself the question, "What, after all, is the greatest common factor in aural pathology?" to find the seemingly simple answer—"Sepsis" and the corollaries of its introduction.

Ninety per cent. of our work, at a conservative estimate, is an effort to control the effects of this enemy, whose only portal of entry is the Eustachian tube.

I therefore thought that a few moments might not be misspent in some study of this phylogenetic legacy of our fishy forefathers. The selection of this subject, too, I realized would give me an opportunity of reminding you of comparatively recent work, to which I wish to draw attention later, and stress in this connection.

With this end in view, I obtained a copy of the passage describing this tube by Bartolomeo Eustachio, the Italian anatomist, from a reprint of the original edition of his work published in 1564, or rather his book dated 1707.

If any apology be needed for such references to the investigations of the past, I would quote no less an authority than that of Adam Politzer, who, in the preface to his comprehensive history of aural therapy, says . . . . "He who would claim complete knowledge in this respect, must learn the work of earlier times."[1]

After a general description of the tube and its anatomical relations, the account by Eustachius proceeds as follows:—

"The portion attached to the apex of the petrous bone is cartilaginous and extremely thick, but the part opposed to this is not cartilage throughout, but has (although I am not quite clear on this point) something of a membraneous character and ends more thinly. Further, at the internal extremity of this passage—which faces the middle of the cavity of the nose—it consists of a strong and more prominent cartilage and is covered by the mucous membrane of the nose and seems to be set as a janitor at the end of the canal. The shape is not round, but depressed somewhat and forms two angles. The breadth of the canal is almost equal to the pen with which we are writing, but at the end is twice as broad as at the beginning and this in like fashion is covered with a thin mucous lining.

"This wonderful provision of nature—which has been discovered by me—in my opinion ought not to be passed over lightly since it can be of no small advantage to both philosophers and doctors, for the more ancient philosophers, amongst whom (as Aristotle reports in 'de Natura Animalium,' bk. 1, chap. 11) was Alcmaeon, perchance thought that goats do not breathe only by the nose and mouth but also by the ears, because they were not ignorant of

[1] ("Wer Anspruch darauf erheben will, sein Gebiet nach jeder Richtung hin zu beherrschen, muss die Leistungen früherer Epochen kennen." *Geschichte der Ohrenheilkunde*, Bd. 1, Vorwort.

the canal which I have described, and therefore would rather often find that the breath, if held, is drawn back by a certain force into the cavity of the ears and as a wave strikes the organs of hearing.

"The knowledge of this canal will also be of extreme value to doctors in their right use of medicines, because in future they will know that even the most dense material can be discharged from the ears, not by narrow ducts, but by a broad passage either by an effort on the part of nature, or by the help of medicines which are called masticatoria." [2]

I am sure you will agree that this description suggests much food for thought and commentary. I had never expected such anatomical and physiological detail, or such suggestion of the great pathological importance of the tube, and it was not a little humiliating to me to find that, even 400 years ago, so many points were recognized which I had intended to emphasize myself.

I would like to direct attention to:—

(1) The accurate description generally. (2) The fact that the tube was described as lined with mucous membrane throughout. (3) That the mucous membrane was continuous with that of the nose. (4) That the pharyngeal end of the tube and its mucous membrane were regarded as a janitor and a wonderful provision of nature, thus protecting the various parts of the middle ear cleft beyond. (5) The stress laid on the point that the knowledge should be of such importance to doctors. (6) The value of mucus and how it can be increased. (7) The inclusion of the phenomenon connected with the so-called experiment usually attributed to Valsalva (though not described by that anatomist till over 100 years later). (8) And finally, the modesty with which, although he claims to have discovered this tube, he acknowledges that Alcmaeon and others some 2,000 years previously must have known of it, and his reason for thinking this.

It is interesting in this latter connection to note that (in 1770) a French commentator on this work was also struck by this character of Eustachius and emphasized the same in the following words: "Although the author was able to claim this discovery as his own, since none of the ancient anatomists had explicitly spoken of this canal, he was not ashamed to quote Alcmaeon who had pointed out that goats breathed through the ears. One is only greater when one renders to each writer what belongs to him. By this act of justice Eustachius has acquired for himself an immortal reputation and no one will deny him the discovery of this canal." [3]

The Alcmaeon quoted, by the way, was not the disreputable poet of that name who murdered his mother, but the philosopher, who lived about 550 B.C., was a

2 (EUSTACHIUS, B., *Opuscula Anatomica*, Lugd. Bat., 1707, pp. 138-140.) Substantia sane ejus, qua extrema fissuræ ossi Temporum et Cuneo simili communis tangit, cartilaginea est, ac admodum crassa; huic vero oppositae partis substantia exacta cartilago non est, sed membranosum nescio quid habet, et tenuior evadit: at hujus Meatus interna extremitas, Narium cavitatis medium respiciens, robusta est cartilago, quae plurimum extuberat, mucosa Narium tunica obducitur, ac fini ejusden Meatus quasi Janitor praefecta esse videtur: figura teres non est, sed aliquantum depressa duos efficit angulos: latitudo cavitatis calamum, quo scribimus, fere adaequat, sed in fine duplo latior est, quam in principio, quae similiter mucosa, sed tenui induitor tunica. Hoc callidissimum Naturae artificium a me inventum contemni (ut opinor) non debet; siquidem tum Philosophis, tum Medicis non parum utilitatis afferre potest; nam antiquiores Philosophi, quorum numero (ut Aristoteles refert primo de Natura Animalium undecimo), fuit Alcmaeon. capras non modo Ore ac Naribus, verum etiam Auribus quoque spirare, forte ob eam causam arbitrati sunt, quod Meatum, quem descripsi non ignorarent, atque adeo saepius experti fuissent, spiritum, ubi ipsum quis cohibet, ad Aurium cavitatem vi quadam impulsum recurrere, et instar fluctus Auditus Organa percutere.

Erit etiam Medicis hujus Meatus cognitio ad rectum Medicamentorum usum maxime utilis, quod scient posthac ab Auribus, non angustis foraminibus, sed amplissima via posse materias etiam crassas, vel a Natura expelli, vel Medicamentorum ope, quae masticatoria appellantur, commode expurgari.

3 (PORTAL, *Histoire de l'Anatomie et de la Chirurgie*, Paris, 1770, vol. i, p. 617.) "Quoique l'Auteur eût pu s'attribuer cette découverte, puisqu'aucun des anciens anatomistes n'avoit directement parlé de ce canal, il n'a point rougi de citer Alcmeon qui avoit remarqué que les chèvres respiroient par les oreilles. On n'en est que plus grand lorsqu'on rend à chaque Ecrivain ce qui lui appartient. Par cet acte de justice, Eustache s'est acquis une réputation immortelle, et personne ne lui a refusé la découverte de ce canal."

disciple of Pythagoras, and is said to have been the first man to have dissected animals as an aid to the study of human anatomy. He also produced a work on the labyrinth of the ear—possibly the first—and influenced the followers of Hippocrates. Unfortunately, though often quoted, his works are lost, and I have been unable to discover why it was thought that goats breathed also through the ears.

Masticatoria were substances chewed to excite the secretion of saliva (which presumably was not then distinguished from mucus) and derived their name from the gum "mastic" used for this purpose.

Now, how far have we progressed? How much use have we made of this knowledge and these stimulating suggestions by Eustachius during the last 400 years?

Naturally, the name of Valsalva will at once be mentioned and his method of aiding hearing by inflation of the middle ear via the tube; but this, as I have pointed out, seems to be wrongly ascribed to him, and further, on reference to his classic work ("De Aure Humana Tractatus," 1707) it is a little difficult to imagine how he has become accredited with this "experiment." It is true that he describes the use of self-inflation, but only as a means of clearing the purulent lesions of the ear, which he stresses at some length, stating that he adopted it as treatment for his "very best patients." It is true also that he realized at least some of the functions of mucus and how tubal obstruction prejudices hearing, but I have sought in vain in this book for any definite description by him of improvement in hearing as the result of self-inflation. I was interested also to find that Politzer had come to the same conclusion in his publication, which I have already quoted. Valsalva was a great anatomist and demands all our respect and honour, but I cannot help reflecting on the difficulties which surround at times, even now, the differential diagnosis between a furuncle, with an intact tympanic membrane, and suppurative otitis media; and visualizing his exhortations to one of his "very best patients," suffering with the former very painful malady, urging him "to blow harder" when no bubbling discharge from the meatus resulted. I must confess to an unholy speculation as to whether a sudden cerebral hæmorrhage resulting thereby in the patient, perhaps gave Valsalva the opportunity of investigating the anatomical causes of apoplexy which he was also the first to describe!

After Valsalva apparently a long gap of 150 years occurred, till Mayer, of Copenhagen (1868), urged the removal of adenoids, as a means, amongst other results, towards relief or cure of otitis media.

Some thirty years later still, Adam Politzer, of Vienna, introduced the use of the air-douche—a method, of course, of very considerable importance. This suggestion, however, was considerably abused, and my own first recollections of the practice seemed to me more with a view to reminding the audience of the advantages of a classical education, as it included an instruction to the victim to commence to decline the demonstrative pronoun, "hic, haec, hoc," when synchronously with the sexless "hoc," compression of the bag was made, and the effect appeared to the onlooker—and must have seemed to the patient—something more like a knock-out blow in the ring than a skilled, deliberate, controlled therapeutic measure of precision.

Fortunately, at the present time, this useful method, with a proper respect, is restricted largely to the cautious, quiet use of the catheter under cocaine controlled by the auscultation tube, and that only after preliminary detailed examination of the nose, postnasal space and ears, and associated with a previous and subsequent test of the hearing.

As to any additional effect by bougies, and the introduction or attempted introduction of medicated oils and vapours, I must confess that I am a heretic, although I know that skilled aurists of repute still use the same.

Later yet, prompted by Killian, we have developed intranasal surgery and have discovered that a structurally normal and healthy nose is of as great importance to the maintenance of hearing, and the relief of some forms of otitis media, as is the removal of adenoids and the provision of a healthy nasopharynx.

But what else has been done? How much further have we advanced in our knowledge of this anatomical structure? How far have we justified the prophecy of Eustachius 400 years ago, that such knowledge should be of great assistance to doctors?

I am afraid we must admit that, with certain exceptions, to which I will shortly refer, our claims are small, though the detailed suggestions of the discoverer certainly merited more attention, and, much more especially, when we reflect that in addition to his then limited methods of investigation, we have had all the advantages which the developments in connection with microscopical histology and physiology offer.

I submit the following as a summary of our present views on the physiology and pathology of the Eustachian tube: (1) It acts as a normal exit for the normal tympanic secretion. (2) It provides a means of maintaining an equality of air pressure on each side of the tympanic membrane, thus permitting an unhindered transmission of aerial vibrations to the inner tympanic wall. (3) It shares in the general congestion associated with acute or chronic naso-pharyngitis, and thus (4) acts as guard against the introduction of septic organisms. (5) As such guard becomes incompetent it constitutes a comparatively easy route for infection of the middle ear, and thus (6) is a large factor in the occurrence of the major portion of aural pathology.

All of which points, on consideration, are merely a transcript of the original description given 400 years ago.

If such summary be admitted, surely we should give more attention to a tract, the efficient control of which should, *ex hypothesi*, also control not only impairment of function, but also the fatal sequelæ of septic infection of the blood-stream and intracranial contents.

From this rather gloomy destructive criticism of the lack of use we have made of the discoveries and teachings of Eustachius and Valsalva, it is a satisfactory relief to be able to refer to some comparatively recent British work in connection with the functions of the Eustachian tube and which I believe points the way to possible progress.

Six years ago, Mr. Lowndes Yates read a paper at the Summer Meeting of the Sections of Laryngology and Otology,[4] which impressed me most strongly, and in which he showed the general action of the cilia and the method by which they controlled the continual flow of mucus, demonstrated that this action was not impaired by the presence of such agents as liquid paraffin, and concluded with a most instructive suggestion as to the mode of infection of both the tonsils and Eustachian tubes from the nose; phenomena that can be easily confirmed by observing the flow of the blood in, e.g., any slight case of epistaxis.

Then in February, 1928, we had a notable paper from Dr. Alexander Fleming, who showed that the tears and nasal mucus are "much more potent than are the common chemical antiseptics in the strengths in which they are employed."[5]

I would submit that these investigations are of paramount importance to us, and should form a very definite milestone in our aim towards protection of the body generally against infection, and the ear in particular. They represent in my opinion the first great step forwards since the first description of the Eustachian tube, and are the first real development of the suggestion made by Eustachius that "the valve-like pharyngeal orifice of the Eustachian tube with its lining similar to that of

4 *Journ. Laryng. and Otol.*, 1924, xxxix, 554.

5 *Proceedings*, 1928, xxi, 859; *Journ. Laryng. and Otol.*, 1928, xliii, 385.

the nose, acts like a janitor for the entry of the middle ear cleft," the knowledge of which fact (as he said) " should be of great benefit to doctors."

But, although we have thus been taught that the provision of mucus and its constant control by the cilial action are physiological phenomena to which attention should be directed, our knowledge of these phenomena is incomplete. We need to know, for instance, how, when, and why the cilial action fails and what is the particular constituent of the mucus which acts as such a drastic deterrent to septic activity.

That mere provision of mucus and cilial action are not sufficient is, I think, illustrated by contemplation of two common ailments, namely otosclerosis and atrophic rhinitis. In otosclerosis, most will agree that the mucous membrane of the nose is abnormally dry and the tube abnormally patent, yet septic otitis media in such cases must be very rare. In atrophic rhinitis, again, the mucus is scanty, whilst in addition the cilial action apparently may be almost absent, yet in this disease also suppurative aural lesions are uncommon.

Obviously there must be other factors, and the mention of atrophic rhinitis recalls the work of Benians and Hayton[6] on the treatment of this ailment—treatment which I have found most helpful—and which was based on an examination of the nasal mucus, and the experimental results of rendering acid its normal alkalinity.

This article has prompted me also to attempt some investigations on the reaction of the nasal mucus, but I have been unable yet to form any definite conclusions as to the correlation of such reaction with health and disease. Further research in this direction may be of value.

I would strongly recommend all these three papers for consideration since they teach us on the one hand, the function of mucous membrane generally, and on the other, how much we owe to this structure for help in our own speciality.

As a result of the work and writings of these three observers, I have restricted my applications for the nose, throat and ears, almost entirely to ointments composed of vaseline and lanoline, or sprays of liquid paraffin.

I have come to the conclusion that these applications combine the best solvent for pus and viscid mucus and the best artificial deterrent to septic activity, with the least disturbance to the local effort of recovery, assisting both in cleansing purulent deposits of the tympanum, when introduced into the external auditory meatus, and in restoring the functions of the Eustachian tube, when introduced into the nose.

They are also almost the only applications I use in the subsequent treatment of mastoid operations after the initial dressing is removed.

The health of the postnasal space and nose is of course of paramount importance. An efficient rhinologist should certainly rob the aural surgeon of much of his work. Indeed, from one point of view, otology consists in dealing with the faults of omission and commission by the rhinologist.

If it be true that 90% of otology is dependent on the action of sepsis—if it be admitted, as of course it must, that, with negligible exceptions, the sole portal of such infection is the Eustachian tube—if we assume that it is only the functional integrity of the lining of this tube which prevents such infection (always potentially present) —then we must certainly concentrate on assistance towards the maintenance of this function of the mucous membrane and its restoration when threatened. It certainly seems to me that our progress in the treatment of aural sepsis must be by preventive measures on these lines.

The necessity for the adequate treatment of the ultimate sequelæ of aural sepsis I wish in no way to minimize. It will of course always be important to learn better how to deal with those dire conditions, suppurative otitis media, labyrinthitis, cerebral abscess, septicæmia, and meningitis, and to recognize the symptoms and signs connected therewith—but I suggest that just as this mucous membrane is a surface structure, so we should not overlook the obvious in seeking the obscure.

[6] *Journ Laryng.*, 1919, xxxiv, 325.

Stimulated by these three recent communications, it seems to me we should be at length in a position to take real advantage of the discoveries of Eustachius and Valsalva, whose teachings can perhaps be summarized as emphasizing the importance of continually recognizing the presence and functions of the Eustachian tube.

I would urge in conclusion that we require further research on these lines, and that our aim should be to provide the individual with a constant efficient mucous secretion.

We must, in accordance with our old well-known dictum, "treat the patient and not the disease," and, if by this means we may be able to avert disease, we shall be able to appreciate more fully the significance of the happy French paraphrase of this sentiment: Il n'y a pas de maladies—il n'y a que de malades."

The Pathogeny of Aural Cholesteatoma.

By Dan McKenzie, M.D.

Aural cholesteatoma consists in the presence, somewhere in the tympano-antro-mastoid cavities, of a congregation of living epidermal cells, which, growing and being shed therein, accumulate to form the cholesteatomatous collections we are all so familiar with. Probably the most usual seat of such cells is the attic-aditus-antrum region. Then comes the mastoid process. Cholesteatoma arising in the lower and anterior part of the tympanic cavity would seem to be exceptional, although it will

Fig. 1.—Aural cholesteatoma showing: (A) Normal bone; (B) connective tissue layer; (C) epidermal cell layer; (D) desquamated lamellæ. (Drawing.)

be found not infrequently to have extended thither. Cholesteatoma beginning in the Eustachian tube I have not yet encountered, nor have I ever heard of it.

The active cells, the essential part of the pathological process, arrange themselves in layers as in the epidermis of the skin, but without papillæ, and they form a more or less extended sheet which rests upon a connective tissue stratum (figs. 1 and 2). Upon the surface of the cell layer are piled its desquamated scales, often likewise

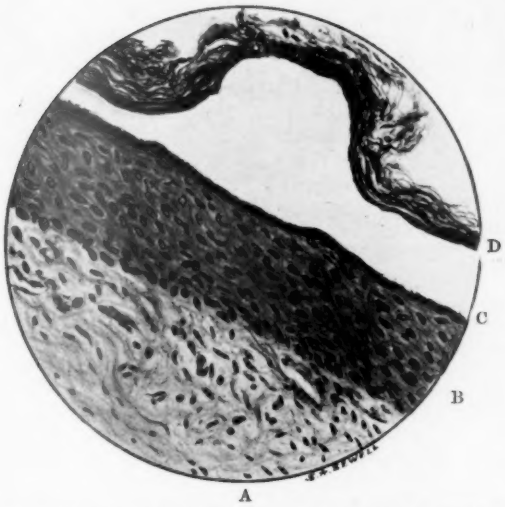


FIG. 2.—Aural cholesteatoma showing: (A) Connective tissue layer; (B) epidermal cell layer; cells proliferating; (C) epidermal cell layer, cells being desquamated; (D) desquamated lamellæ Drawing.)

in fine continuous sheets or lamellæ (fig. 3), which, if the cholesteatoma remains closed, may accumulate as in a cyst, to form an ever-expanding tumour, but which, if given time, will ultimately break through the containing fibrous or bony wall. Thus the extent to which the cholesteatomatous mass will reach is incalculable.

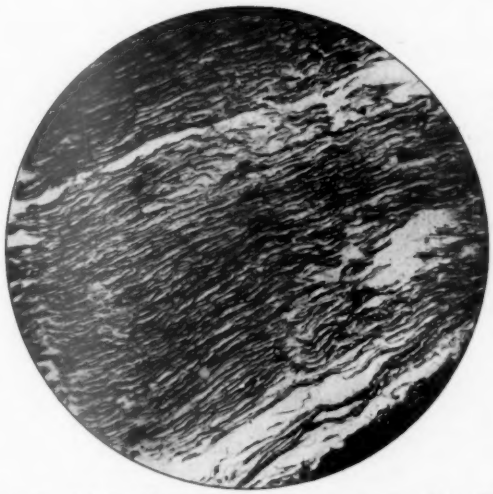


FIG. 3.—Lamellæ of shed epidermis from cholesteatomatous cavity. (Photograph.)

The problem before us is: how do growing epidermal cells get inside these cavities?

In answer to that question a number of theories have been propounded, but they may be conveniently divided up into two: first, those which attribute the presence of epidermal cells in the ear-spaces to the effect of suppuration of the middle ear—the so-called "secondary" cholesteatoma; and secondly, those which regard cholesteatoma as arising independently of suppuration—the "primary" cholesteatoma.

As a matter of fact, all authorities agree that primary cholesteatoma has a real existence; that it sometimes forms without any antecedent suppuration. But ruling otological opinion holds that this variety is extremely rare, and that secondary, or, as we may call it, suppurative cholesteatoma is the usual variety.

(It will facilitate our exposition if we reverse formal procedure and begin with secondary cholesteatoma, reserving our discussion of primary cholesteatoma until the latter part of the paper.)

Of the manner in which the secondary cholesteatoma may originate there are three different accounts to hand, all of which we shall consider. These are (1) the immigration method; (2) the transformation method (or metaplasia) through the effects of (*a*) suppuration or (*b*) desiccation.

IMMIGRATION.—(This theory we owe to Bezold and Habermann, working independently of each other; but it was adopted and reinforced by Politzer, through whose advocacy it spread and through whose influence it still remains what we may call our classical teaching.)

According to Politzer, aural cholesteatoma, in the great majority of cases, is produced by the ingrowth of the epidermis of the external auditory meatus into the tympanic cavity through a perforation in the tympanic membrane. He points out, however, what must strike everybody, that epidermis is not likely to invade the tympanum in the face of virulent sepsis or profuse suppuration. Further, if, on the other hand, purulent otitis media is undergoing cure and epidermis spreads into the tympanum, it does not then tend to form a cholesteatoma. All that happens is, that it assists in the cicatrizing process; and there it stops. Thus, an invasion of the middle ear by epidermis will only lead to cholesteatoma formation under the strictly limited condition of mild sepsis.

As to the behaviour of the invading epidermis towards the tympanic epithelium, Politzer makes two distinct observations, which are combined into one by him as follows:—

> "Either the stronger epidermis of the canal presses before it the less resistant epithelium of the tympanum—where this is present—or else it passes over spaces devoid of this epithelium."

But a remarkable development of the argument follows. As Politzer clearly saw, and as he clearly pointed out, cholesteatoma is found much more often in the attic-antrum region than in the anterior part of the tympanum. It is, indeed, as we all know, typically associated with that so-called "perforation" that lies at or near the edge of the upper and posterior quadrant of the tympanic membrane. Here Politzer found himself confronted with an awkward fact. If, as he said, cholesteatoma could be produced by epidermis invading the tympanum through a perforation in the membrane, why does it not pass through an anterior perforation as readily as through a posterior perforation?

THE MARGINAL PERFORATION.—This difficulty he managed to surmount by an ingenious device. In a central perforation, said he, the epidermis in contact with the tympanic mucosa is only epidermis of the membrana, and so it is not strong enough to spread, whereas the posterior perforation is a marginal perforation, and the epidermis contiguous to it, being meatal epidermis, is stronger and more prolific than membrana epidermis, and so is capable of invading the tympanum. He went so far as to lay it down as a rule that marginal perforations are more likely to lead to

cholesteatoma than central perforations. And this dictum of the master has been repeated since his day by every teacher of otology, including the writer of this paper.

And yet, as a moment's consideration will show, to elevate this argument to the height of a generalization, almost you would say a natural law, is unwarrantable, for the simple reason that the postero-superior perforation is unique in being marginal. Everywhere else, all around the tympanic membrane—the membrana vibrans at least—wherever a perforation may form, even when the entire membrana vibrans is destroyed, the destruction fails to reach the margin, because the annulus tendinosus persists. (To this statement there are no doubt exceptions, but they are so few as not to invalidate it.) That is to say—and here we reach the central point of our criticism—the postero-superior perforation is something individual and peculiar. It differs from all others, as we have just said, in being marginal. This, no doubt, is partly owing to the fact that it usually involves Shrapnell's membrane, where there is no annulus tendinosus; but not entirely so, since it may also implicate the adjoining part of the vibrating membrane, where in like manner it is marginal. What happens here is, that the bone supporting the annulus tendinosus is destroyed, and with it this tough barrier between the tympanic epithelium and the meatal epidermis.

That is to say, the postero-superior perforation frequently involves a destruction of the bone at this part of the osseous meatus. Sometimes, indeed, as we know, the destruction is limited to the bone, and the membrana itself shows no loss whatever.

Herein lies its distinction from all other perforations, and I ask the reader to remember this point, for we shall be returning to it.

THE POSTERO-SUPERIOR MEATAL EPIDERMIS.—We are now in a position to return to the strength of the meatal epidermis, and to Politzer's further and curiously discriminating claims therefor. He says:—

"With perforations of the pars flaccida the invasion takes place the more easily, because a more highly developed band of cutis and epidermis extends from the superior wall of the meatus to the membrana tympani; in other words, a more intensive growth of epidermis is found at this part than in the other parts of the meatus."

And again:—

"The migration of epidermis is facilitated in marginal perforations, especially in the postero-superior quadrant and in Shrapnell's membrane, where a stronger strip of epidermis impinges upon the membrana tympani."

May I say that, when, after much pondering, I came to appreciate the implications of all those statements about the meatal epidermis, I began at last to realize what extraordinary flights are necessary for the support of the immigration theory of cholesteatoma. For this theory, as we now see, depends upon the relative strength, not only of meatal epidermis towards tympanic epithelium; not only of meatal epidermis towards membrana epidermis; but actually of one particular strip, the postero-superior meatal epidermis, towards the epidermis of all the other meatal walls.

It is true that the skin lining the roof of the meatus is said to be somewhat fuller and thicker than elsewhere; but to credit it with prolific qualities so superior to all its neighbours as the foregoing statements demand, throws a severe strain upon one's credulity; and the strain is not reduced when we are virtually asked to believe that the only strip of epidermis capable of producing cholesteatoma is by an inscrutable dispensation of Providence led up to the only perforation capable of utilizing it.

What reason have we to suppose, apart from its hypothetical powers as an invader, that this strip is any "stronger" than its neighbours? And if we are relying upon its invading powers as the proof of its strength, are we not simply begging the question?

CHOLESTEATOMA OF THE MEATUS.—It is, as a matter of fact, easy to see from his writings what it was that led Politzer to insist so much upon the rôle of the meatal epidermis. Two factors influenced his judgment; one was desquamative external otitis, or, as it used to be called, cholesteatoma of the meatus, and the other was his interpretation of the naked-eye and microscopic appearances of cholesteatoma in the middle-ear spaces. We shall take these one after the other.

In desquamative external otitis, successive layers of epidermis are exfoliated in sheets which accumulate in the deep meatus and may, by pressure atrophy of its bony walls, lead to an extraordinary dilatation of its lumen. The resemblance of this disease to antro-tympanic cholesteatoma is, of course, very close. The old name indeed is in a sense quite correct. What more natural then, than to argue from the visible and known meatal cholesteatoma to the concealed and unknown antro-tympanic cholesteatoma, and to regard the latter as on all-fours with, and as it were an extension of the former?

But resemblance, however close, is not necessarily identity, and although Politzer speaks of an "excessive production and desquamation—especially in the external meatus" as a feature of the "secretory stage" of chronic middle-ear suppuration, in the few cases of desquamative external otitis that I have seen (it is a rare disease) there has never been any suspicion of past or present suppuration of the middle ear: and, in spite of the great hollowing out of the deep bony meatus, the tympanic membrane has always been intact. I have never, that is to say, seen cholesteatoma of the meatus extending through a perforated tympanic membrane into the middle ear. I may also add that, as far as one could determine, the postero-superior area of the deep meatus did not seem to be any more prolific of desquamated products than the rest of the canal. Indeed, according to my observation of a recent case, the floor of the meatus shows more activity in desquamative otitis externa than the roof.

OBJECTIVE EVIDENCE OF IMMIGRATION.—The appearance presented by aural cholesteatoma was first interpreted as invasion of meatal epidermis by Bezold and Habermann. Politzer agreed with their views, and quite recently Nager, of Zurich, has added his testimony to the same effect.

In certain of their specimens, it seems, they saw the meatal epidermis continuous

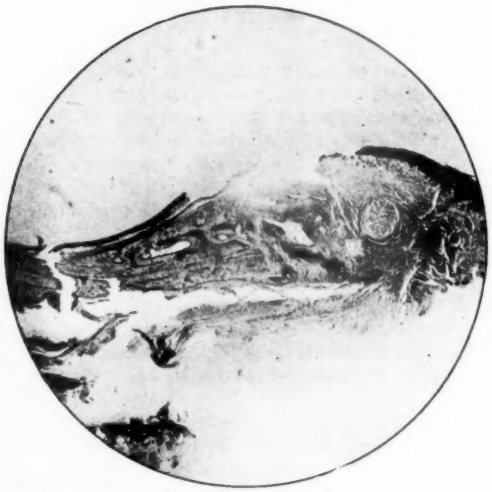


FIG. 4.—Edge of cholesteatomatous lining membrane on bone, integument on right. (Photograph, low power.)

with the cholesteatomatous lining passing some little way into the antro-tympanic cavity and coming to an abrupt stop. In one instance, reported by Politzer as showing "undoubted invasion," it had "pushed in" the tympanic mucosa.[1]

That being so, what else could they think but that what they were looking at was meatal epidermis pushing its way into the tympanum?

But notice how we have described the appearances: "Meatal epidermis continuous with cholesteatoma lining passing into the cavity and coming to an abrupt stop," while the tympanic mucosa is "pushed in." The phraseology describes a movement, and a movement from without in. But suppose we reverse the movement. Suppose we say: "You can see the cholesteatomatous lining passing out to unite with meatal epidermis as it does when spontaneous cure of cholesteatoma occurs"; and, "the tympanic mucosa is seen to have been pushed aside by an expanding cholesteatoma"—what would be the reply to that interpretation of the appearances?

The truth is, of course, that each of those conflicting views expresses more than the appearances warrant. Each of them imparts progress to a static situation, no uncommon error in pathology!

But, since, as I have shown, it is as easy to see cholesteatoma passing out as it is to see epidermis pressing in, the objective evidence in favour of invasion turns out, after all, to be merely subjective!

Looking back now over our criticisms of the immigration theory, I think we can claim that they have been rather damaging.

We must not forget, however, that epidermal invasion of a sinus track is a well-known pathological phenomenon. There is nothing inherently impossible in the suggestion. All we are concerned with is whether invasion is responsible for aural cholesteatoma, and our chief difficulty in assenting to this solution is furnished, as we have seen, by the favourite location of the disease being the upper and back part of the tympanum.

We shall have further criticisms to make as we proceed.

METAPLASIA.—(A) *From suppuration.*—We now turn to the other explanations of the method by which suppuration of the middle ear may lead to cholesteatoma formation. The first is, that the epithelium of the middle ear may be transformed into stratified squamous epithelium by a change in its own constitution through the irritant effects of long-continued suppuration.

Such a change from such a cause is, apparently, not to be denied. At all events, both clinical and experimental evidence goes to show that there is nothing eternal and unchangeable about epithelium; that a transformation from columnar, say, to squamous epithelium is quite an everyday consequence of slow irritation. A metaplasia to the keratin-forming cells that give rise to cholesteatoma, therefore, can be easily imagined.

If we may judge from the discrepant accounts of the various authorities, the epithelium of the middle ear presents considerable variation in different subjects. But it seems for the most part to be ciliated columnar epithelium in the lower part of the tympanum (showing papillæ, according to Brühl and Politzer's "Atlas"), while on the roof, promontory, ossicles, inner aspect of the membrana and mastoid cells, it consists of a single layer of cubical or of flat pavement epithelium.

In view of the acknowledged propensity of mucous membrane epithelium in general to assume the stratified squamous form as a reaction to chronic irritation, probably the cylindrical is just as liable to the change as the pavement type. Nevertheless, it is natural for us to suppose that the latter would probably undergo metaplasia more readily than the former. This consideration, coupled with the knowledge that these more easily changing cells are situated in the upper tympanum

1 This must have been a non-suppurating middle ear, as it is recorded that "no other pathological change in the middle ear was visible." The significance of this interesting fact seems to have escaped the author.

and mastoid, renders the suppuration theory more plausible than the immigration theory, since it can account for the preference shown by cholesteatoma for the upper and back parts of the tympanum without invoking such a *deus ex machinâ* as that strong strip of meatal skin.

The only objection to it, apart from certain clinical phenomena to be considered presently, is that it seems to afford rather too ample an opportunity for cholesteatoma formation. In other words, we ought to be able to explain how it comes about that many people with long-continued suppurative otitis media contrive to escape cholesteatoma.

Until this can be done, the suppurative theory also must be regarded with considerable doubt.

METAPLASIA.—(B) *From Desiccation.*—The second theory of metaplasia is that of Wyatt Wingrave, namely, that the transformation may be due to desiccation of the aural epithelium. With metaplasia from this cause, he reminds us, pathologists are already familiar in prolapse of the rectum and uterus, and, in our own regions, in the nose. If, then, we have a sufficiently large perforation in the membrana, the vapour tension in the air of the middle ear will be lowered, and, as a consequence of evaporation from its mucous lining, the surface will become dry and the epithelium squamous.

This differs from the immigration and active suppuration theories in necessitating a dry tympanum. Desiccation can scarcely occur if the surfaces are kept moist by discharges. But it is one of the secondary theories nevertheless, since it postulates a previous suppuration.

Now there is no doubt whatever that desiccation does take place in the presence of a healing or healed suppuration with a permanent perforation in the membrana. Indeed, when we are treating those cases, we do not feel satisfied until the inner tympanic wall has become quite dry.

But the difficulty in accepting Wingrave's view lies in the clinical fact that we do not find cholesteatoma developing in cases with healed suppuration and an open perforation. In many of these, to be sure, cicatricial webs and bands form between the membrana and the inner tympanic wall and shut off the greater part of the tympanum from the outer air. But in others, the perforation through the membrane is not thus sealed; there is, to all appearance, free communication between the air of the external meatus and that of the antro-tympanic spaces; and yet cholesteatoma does not eventuate.

Such, then, are the most reputable of the explanations that have been offered to account for the genesis of cholesteatoma when it is presumed to be secondary to chronic suppuration of the middle ear. Of the three, the second, that the epidermal cells in the middle ear spaces are the result of a metaplasia due to the simple irritation of prolonged suppuration, would appear to be the least open to objection. The immigration theory requires a whole series of hypothetical assumptions that wither up under searching criticism, while the desiccation theory is weak on the clinical side.

PRIMARY CHOLESTEATOMA.—As we remarked in the introduction, no one doubts that cholesteatoma may form in the temporal bone without any previous suppuration. Every otologist of experience has encountered, though it may be but rarely, cases in which he has come upon a roundish cholesteatomatous collection embedded in the mastoid process, with an opening usually through the posterior wall of the osseous external meatus close to the isthmus. Granulations, sometimes polypoid, spring from the edge of the fistulous opening in the bone. The deeper meatus is full of cholesteatomatous débris, but when it is cleared out the membrana tympani is seen to be intact and the hearing is normal. When it is operated on, no route can be discovered leading from the cavity of the cholesteatoma

to the antrum or middle ear: Unmistakable primary cholesteatoma; isolated; independent; self-sustaining; a neoplasm in short.

Confronted with such a case some fifteen years ago and forced by its discovery to reconsider the whole problem of aural cholesteatoma, the logician within me was irresistibly reminded of Occam's razor: *Entia non sunt multiplicanda præter necessitatem*, which may be rendered for our present purposes by: Why assume that there are two varieties of cholesteatoma when one, the primary, will suffice?"

In other words, Is cholesteatoma ever a sequela of suppuration? Is it not more likely that cholesteatoma of the temporal bone forms inside otherwise normal tympano-antro-mastoid cavities without any antecedent suppuration; that in its growth and expansion it erodes the bone of the external meatus and/or the membrana from within; that there is thus an e-migration and not an im-migration; and lastly that suppuration of the middle ear, if it occurs, is a sequela of the cholesteatoma, and not vice versa?

In order the better to appreciate the bearing of facts upon these suggestions we shall now proceed to examine cholesteatoma more in detail; first, in its structure; secondly, in its effects upon its environment; thirdly, in its clinical manifestations. Finally, we shall endeavour to account for the presence of cholesteatoma inside the closed temporal bone.

STRUCTURE OF CHOLESTEATOMA.—The secret of the behaviour of cholesteatoma lies in the epidermal cell layer of the cholesteatomatous membrane. This consists usually of several rows or series of cells, like those of the rete Malpighi of the skin, passing from the deeper columnar or spherical cells to the surface squames. They behave like the epidermal cells of the skin: proliferating, coming to the surface, being shed, and then accumulating one on top of the other if they cannot find an exit.

Interposed between the normal tissues and this layer or coat of active cells, which, like the epidermis, contains no blood-vessels, is a fibro-vascular layer manifesting for the most part the characters of normal connective tissue. (Figs. 1 and 2.) Papillæ are absent. Sections often show the fibro-vascular layer separated from the cell layer, but when the cholesteatomatous membrane is peeled off bone, both layers come off together (fig. 5), so that their union must be close.

Both of these two coats vary considerably in thickness in different cases. (Cf. fig. 5 and fig. 7.) The flattened appearance of the thin lining in figs. 7 and 8 suggests the action of pressure. (To this we shall return later.)

Several reports about the cholesteatomatous lining require comment.

It is sometimes said, for example, that cholesteatoma, even a large cholesteatoma, may be found without any membrane whatever. To such a statement I dare not give an absolute denial; it is made on good authority. I should like, however, to offer two remarks thereanent: First, that every greyish-white pultaceous mass in suppurating cavities is not cholesteatoma; some consist of decomposed pus and are merely caseous material. Secondly, so far as I myself am concerned, I have never yet failed to find membrane in cholesteatoma. The shred has sometimes been small, but it has always been found when looked for.

Again, the lining is sometimes found when examined microscopically to be devoid of epidermal cells. But caution should be exercised not to assume from such limited observation that the whole of the membrane in the case is acellular. Nevertheless, if it were found to be so, the fact need not surprise us, since the increasing accumulation of shed epidermis in the closed, cyst-like growth may so compress the living epidermal layer, particularly where it lies upon bone (fig. 7), as to lead to its atrophy.

It is noteworthy that the normal tissues, bone and connective tissue, beneath the cholesteatoma in the sections shown, betray no evidence of any inflammatory reaction. We shall return to this interesting point later.

The familiar whitish cholesteatomatous material that constitutes, as a rule, by far the greatest and bulkiest part of the cholesteatoma is, of course, the dead and

FIG. 5.—Detached cholesteatomatous lining. Section shows connective tissue layer cut on flat. (Photograph, low power.)

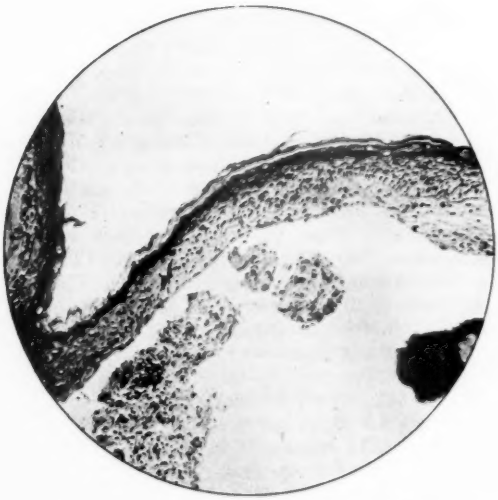


FIG. 6.—Detached cholesteatomatous lining. H.P. to show connective tissue layer; epidermal cell layer (note palisade cells); and desquamating lamellæ. (Photograph.)

desquamated product of the epidermal cell layer. In its primitive, unspoiled state it consists of fine wavy sheets or lamellæ, closely packed together (fig. 3), some of which compacted to form a "pearl" may occasionally be found.

FIG. 7.—Cholesteatomatous lining (epidermal and connective tissue) on normal bone. Flattened by pressure. (Photograph, low pressure.)

FIG. 8.—Cholesteatomatous lining (epidermal and connective tissue layers) on bone. Flattened by pressure. Bone normal. (Photograph.)

Now, if we take these three constituents of cholesteatoma as they appear in the indubitably primary disease, we shall find that they form a cyst-like tumour, the walls of which with their connective tissue and active growing cells, enclose as in a

capsule the ever-increasing mass of desquamated lamellæ. In the mastoid the tumour occupies a cavity in the bone which it has excavated, and it is quite clear that so long as the cyst remains closed it will remain aseptic.

THE TWO VARIETIES OR CONDITIONS OF CHOLESTEATOMA.—When, however, we open into a cholesteatoma connected with the ear-spaces, if these are suppurating, we shall often find the main mass to be pultaceous, amorphous and disintegrated. Microscopically, lamellæ may here and there be visible, or they may be broken up into a granular detritus, in which, however, squamous cells are still easily recognizable. Yet, even in this state, as I have already said, the lining membrane can be found, although it may not now be enclosing the desquamated material like a cyst-wall. Its integrity seems to be preserved longer when lying on bone than when in contact with soft tissues, or when devoid of any external support.

Thus we encounter cholesteatoma at our operations in two states, first, the circumscribed, cyst-like cholesteatoma, with easily recognizable elements; and second, the structureless, broken-up mass of more or less loose detritus.

Now, here again we come across a view-point of Politzer's that requires close scrutiny. Politzer looks upon those two conditions as being two entirely separate varieties of the disease, differing both in origin and in character. And, from my reading of his descriptions, although he does not expressly state his opinion in so many words, I take it that the latter, the disintegrated variety, is that which he regards as being due to epidermal invasion, while the former he looks upon as spontaneous or primary cholesteatoma.

To enter more into detail, according to this way of looking at these two conditions, it seems that, on the one hand we have a cyst-like, self-contained tumour; on the other hand, we have an open area of the antro-tympanic cavity, carpeted merely, to all appearance, with cholesteatomatous membrane. If that distinction is correct, and if the latter represents the secondary cholesteatoma, resulting from invasion, then one would expect its gradually accumulating débris to ooze about in all directions, filling up not only the external meatus, but all the accessible cavities in the temporal bone. Now, although we quite frequently find the amorphous cholesteatoma occupying relatively extensive areas, filling the tympanum, e.g., yet we do not meet with cases in which the whole of the available cavities are filled as from a reservoir, the bony septa being left standing.

What we do find, even in the most open kinds of cholesteatoma, is that the material is concentrated in one quarter or region, and we generally also find this quarter converted into a unilocular cavity, as if it had once been occupied by a cyst or a tumour. In other words, cholesteatoma always presents a nidus.

Thus there is another way of regarding those two types of cholesteatoma: namely that they are merely two stages in the history of all cholesteatomata; that the amorphous variety is nothing more than the circumscribed or encysted variety which has come into communication with the external air, and has undergone decomposition; that change taking place after the cholesteatoma has eroded the bony meatal wall, or the tympanic membrane, or both. That this is what occurs is supported by the fact, imparted to me by Wyatt Wingrave, that closed cholesteatomata are devoid of fœtor.

Now a consideration of the detailed pathological appearances and clinical happenings in cholesteatoma enables us to map out what occurs when air obtains access to a closed cholesteatomatous cavity. The consequences show some variety. In all cases, the central mass undergoes decomposition as we have seen, owing to the entrance of putrefactive bacteria. But, contrary to general opinion, the influence of pathogenic bacteria on the disease area may be quite trifling. Their effect seems to depend upon whether or not the normal tissues are exposed to their action. Thus the bare edge of the bony fistula, as we saw, frequently becomes infected so that granulations and polypi sprout up. But the tissues directly underneath the

cholesteatomatous membrane do not seem to become readily infected. The membrane appears, indeed, to act as a graft does when it is applied to the raw bone surfaces after a radical mastoid operation; it shields the underlying bone from attack by the organisms of sepsis.

It may seem surprising to talk of an open cholesteatoma without suppuration, but Wingrave has shown, and any clinician can test the matter for himself, that in many cases of cholesteatoma discharging into the meatus, the discharge from the ear is non-purulent, consisting only of serum with epidermal scales. Nay, this kind of non-purulent discharge is often present in cholesteatomata with the marginal perforation. That is to say, we may actually have a cholesteatoma of the aditus-antrum region discharging into the meatus without any suppuration either of its own area or of the middle ear: a fact difficult to reconcile with the idea that cholesteatoma is, except in the rarest circumstances, always secondary to suppuration of the middle ear.

In most of the sections shown in the figures appended there is no evidence of infection in the area underlying the cholesteatomatous membrane; and in the many sections of bone taken from the walls of cavities the bone is normal to all appearance. (One section shows some leukocytic infiltration into the sub-epidermal connective tissue, obviously recent.)

Now if this reading of events is correct, so long as the cholesteatoma, regardless of its position, remains enclosed, there will be no suppuration either in its own area or in its neighbourhood. It may even be situated inside the tympanum and yet give rise to no suppuration. Further, if it erodes its way into the external meatus, so long as it presents an intact wall towards the middle ear there will be no suppuration of that cavity.

If, however, in its expansion, the cholesteatoma, having opened into the meatus, ruptures also into the tympanum so that its débris is scattered about therein, suppuration may be expected. Or, what appears to be more common, if in its expansion it produces a bare edge of eroded bone, that edge is very liable to become carious. In this way is to be explained the discrete character of the lesions associated with cholesteatoma. Thus, as we all know, the bone of the attic wall may be raw and carious, while the membrane and ossicles are apparently altogether free from disease. There is, generally, something distinctive and characteristic about cholesteatomatous septic infection and suppuration.

Now, the clinical outlines sketched in the last few paragraphs, if we exclude the allusions we have made to the middle ear, would be accepted by most if not all authorities as correct for those cholesteatomata that open into the outer part of the bony meatus at a distance from the membrana. But the same kind of evolution is rejected if the cholesteatoma lies close to, or inside the tympanic cavity. Why so? Surely to assume that there is a fundamental difference between a cholesteatoma opening at the isthmus and a cholesteatoma opening at the membrana is, shall we say, doing violence to probability.

Expansion of the Cholesteatomatous Cavity.—Meantime, it is to be noted that, according to our views, the changes that take place in and around an enclosed or cystic cholesteatoma, are non-inflammatory, consisting chiefly in the absorption of the bone wall and the consequent expansion of the cavity in which the cholesteatoma lies.

The method by which the bone is absorbed has also been the subject of debate. It is generally attributed to the pressure of the expanding mass. This we can admit without any difficulty in the case of a closed cholesteatoma. But, at first sight, it is less easy to accept it as occurring in an open cholesteatoma. The fistulous opening ought, one would think, to relieve the pressure. But, as a matter of fact, the fistulous opening may fail to do so. In desquamative external otitis,

for example, dilatation of the bony meatus occurs although the canal remains patent. For both in that disease and in open cholesteatoma the opening may be insufficient to afford relief to the pressure exercised upon the rigid bony walls by the accumulating lamellæ.

Again, although we sometimes find that when we break into a cholesteatomatous cavity (with a meatal fistula) during operation on the mastoid, the contained material bulges up under manifest pressure into the breach made with the gouge, yet there are many cases encountered in which no such protrusion appears. The only solution we can offer is that in the latter the pressure has been relieved in some way before operation. Some of the difference may be accounted for by the physical state of the contents of the cavity. If much liquefied they will be voided and the pressure lowered.

Yet, at the same time it must be admitted that the existence of massive pressure is difficult to imagine in open cholesteatomatous excavations of the type shown to-day by Mr. Graham Brown, in which the radical mastoid operation is performed by Nature. Is it possible that the cholesteatomatous epidermal layer itself in its growth exercises a local pressure upon underlying bone?

Two possibilities other than pressure-atrophy of the bone may be mentioned. One that occurred to me some time ago, has also been suggested by Steinbrügge, and more recently by Lautenschlager; and that is that the epidermal cells may, like osteoclasts, exercise a chemically solvent action on the bone upon which they are lying. Animated by this idea I asked Dr. Arnold Renshaw to investigate the reaction of cholesteatoma. But it was found to be uniformly alkaline, doubtless from ammoniacal products of putrefaction. The suggestion is, in any case, negatived by the fact that the living epidermal cells are not in immediate contact with the bone, the fibro-vascular layer lying between them (fig. 1).

KIRCHNER'S HAVERSIAN INVASION.—This brings us to consider a demonstration by Kirchner before the Otological Section of the International Congress of Medicine at Berlin in 1891, since, if he is correct, the epidermal cells of cholesteatoma do come into contact with bone. Kirchner showed sections in which he described both epidermal cells and cholesteatomatous detritus inside the Haversian canals of the bone in the neighbourhood, where their action, whether mechanical (as he held) or chemical, would certainly lead to absorption. Kirchner's findings were corroborated by Kuhn, and accepted by the President, Prof. Politzer, the last-named remarking that cholesteatomatous membrane, when removed, presents club-like protrusions on its outer aspect, that is to say on the aspect next the bone. These authorities connect this invasion of the bone with the well-known tendency for cholesteatoma to reappear after attempts at removal. Kirchner, indeed, draws a parallel between the behaviour of cholesteatoma in respect of recurrence and that of a malignant growth. (I should like to underline this *obiter dictum* of Kirchner's for a reason which will appear in our concluding remarks.)

With regard to his demonstration of Haversian invasion, however, it would appear that, as far as I can learn, those observations of his have not been repeated by later workers. Doubt, therefore, and, in my opinion, reasonable doubt, has arisen regarding their accuracy. I may say that I have sought in vain for epidermal cells within the bone in the sections I have seen; and in the second place, that the cholesteatomatous membranes I have examined have always been smooth. Flat, mound-like protuberances (fig. 9) are usual, but one can scarcely call them club-like. Again, in order to reach the bone, the epidermal layer would have to penetrate the interposed fibro-vascular layer in the manner of an epithelioma. Further, an appeal may be made to the experience of the operating otologist. We have all observed the smooth, shallow, saucer-like depressions in the bony wall of a cholesteatomatous cavity after the removal of its lining; the mounds mentioned above are, by the way, obviously the counterpart of these depressions.

Now, if the bone were penetrated as described by Kirchner, its surface would not be smooth; it would be dotted over with a multitude of small pits; it would be cribriform. Finally and conclusively, clinical observation shows us that the cholesteatomatous membrane may be left undisturbed in suitable cases, not only without risk, but with advantage, to act as a graft, as Sir James Dundas-Grant has pointed out. Subsequent recurrence in such cases does not seem to be the rule.

FIG 9.—Recent cholesteatoma showing lobulated surface. (From the late Dr. Neil Maclay, Newcastle.)

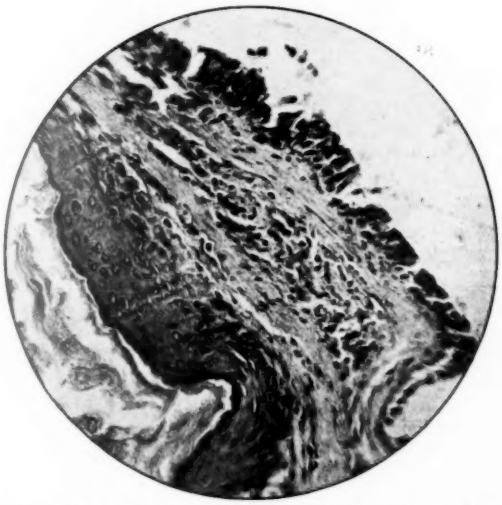


FIG. 10.—Wall of cholesteatoma cyst (from healed radical mastoid cavity) showing cholesteatoma lining (on the left) "back to back" with tympanic epithelium (on the right) (from the region of sinus tympani). (Photograph, × 100.)

No doubt we have all seen cholesteatoma recur after a radical mastoid operation, to form a true cholesteatomatous retention cyst, a section of one of which is shown here (fig. 10). But this cyst, Dr. Scott Williamson thinks, has been produced from a nest or clump of cells on the surface of the bone that has escaped the curette.[2]

[2] Kirchner's sections, we ought perhaps to remark, were stained with picro-carmine, and pathological authorities I have consulted regard this stain as misleading. In any case, to detect epidermal cells in a canal as small as a Haversian canal must surely be regarded as an unusual microscopic feat.

We are thus, for want of anything better, thrown back upon pressure atrophy (fig. 7). The important point for us is that the bone absorption at this stage is an aseptic process. After the cholesteatoma is open, however, as we have already remarked, septic infection may pass to the underlying tissues if they have been denuded of the cholesteatomatous covering. Thus we occasionally see granulations sprouting up through the cholesteatomatous membrane into the cavity.

Before taking leave of the subject of the absorption of bone, however, I should like to say that I have often wondered whether the characteristic denudation of the dura of the middle fossa is the result of massive pressure atrophy or of caries. It must be due to penetration of some kind, as the inner table is broken up into minute granules that feel like sand or grit when rubbed between the fingers. But as they are held together by fine granulation tissue (fig. 11), Dr. G. Scott Williamson considers that they are due to simple aseptic pressure. He has informed me that

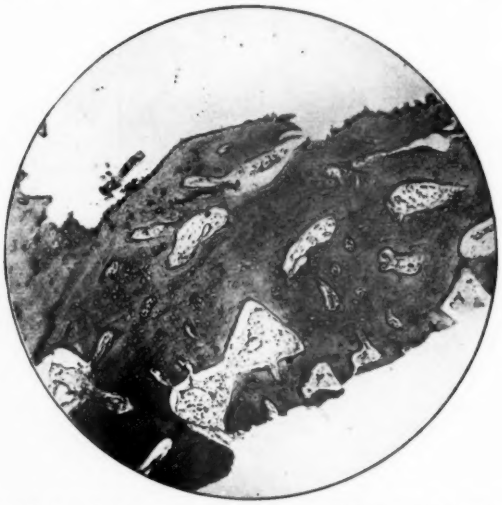


FIG. 11.—Aural cholesteatoma. Granule of bone-grit from roof of antro-tympanum. Aseptic pressure-atrophy. (Photograph L. P.)

he has seen a similar appearance produced by tumours of the ethmoid eroding their way into the cranium. The breaking up and absorption of the bone are brought about, he tells me, by the dura. Presumably the familiar fistula of the lateral semicircular canal is produced in the same aseptic manner.

On the effect of the expansion of the cholesteatomatous cavity and the atrophy of bone in exposing important structures there is no need to linger. But it is worth while noting that the cavity may be very large. Cholesteatoma forming a direct connection—a bridge—for the conveyance of septic infection from the external meatus to the middle ear, to the lateral semicircular canal, to the lateral sinus, and to the brain is the pathological feature which gives to open cholesteatoma its sinister importance.

Now, in these conditions, we have to deal with a cholesteatoma which has made an internal breach, not only in its bony envelope but also in its own proper wall or capsule. But the process by which the internal breach is made must be the same as that which leads to the formation of the fistula in the external meatus, namely,

first of all an erosion of the bony wall, and then as this rigid support is lost an exposure of the underlying soft tissues, and we must assume a rupture of the cholesteatomatous lining or capsule. Moreover, when the cholesteatoma is enlarging into a free space, rupture of its wall will obviously be likely to occur at the spot where it loses the support of the normal tissues around it. It is to be noted that, if our account of this evolution of change is correct, an internal breach will not lead to infection unless the cholesteatoma has also an external opening into the meatus or elsewhere. This external opening may either precede or follow the formation of the internal breach. It may be mentioned, and a case illustrating the fact will later be narrated, that widespread conveyance of infection may be effected by a cholesteatoma devoid of a meatal opening through nasopharyngeal infection setting up an acute otitis media, and passing thence to infect a cholesteatoma previously free from sepsis.

The point is, that a cholesteatoma may show no septic reaction in its own walls but may nevertheless convey sepsis to infect the less resisting tissues it has exposed.

Thus the most important breach in the cholesteatoma is the formation of the fistula or sinus into the external auditory meatus. To this particular lesion we have already devoted a great deal of attention.

This is the commonest of all cholesteatomatous openings. Moreover, it is a fistula that is frequently formed by a comparatively small cholesteatoma, a fortunate event, since it then erodes its way into the external meatus before it has extended so far as to endanger any of the deeper structures. When the fistula is relatively large enough to permit of an extrusion of all the dead cholesteatomatous débris, spontaneous cure may occur, the lining acting like a graft, as in Dundas-Grant's cases, while its edge unites with the meatal epidermis to cover the bony edge of the fistula, one of the weak points, as we have seen, in the tissue defence. The occurrence of natural cure, in this way, is well known.

It is significant, as a point in favour of the primary theory, that we not infrequently come across healed marginal perforations in people who have never even suspected that they had had anything wrong with the ear. (We shall be returning to the marginal perforation in our concluding paragraphs.)

CLINICAL EVIDENCE.—There are certain other clinical phenomena that favour the primary genesis of all cholesteatomata. Everyone must have noticed, for instance, how seldom cholesteatomatous patients give the history of an acute onset of their disease, with pain and the sudden appearance of purulent discharge. As a matter of fact, when such a story is given, we generally find it to be recent, the acute symptoms being the effect, not the cause, of cholesteatoma—for that disease, like tuberculosis, generally begins imperceptibly, apart from the appearance of a scanty, fœtid discharge.

Again, speaking for myself, I have to say that I have never been able to assure myself that I have actually observed a simple chronic suppuration gradually changing its character and becoming cholesteatomatous. Is it not the fact, indeed, that that disease is fully formed and displayed when we first see it?

Further, it may be urged that if the evolution of cholesteatomatous suppuration of the middle ear follows the course described above of cholesteatoma preceding suppuration, then we ought surely to be able to cite cases in which a closed cholesteatoma is accidentally discovered in the antro-tympanic cavities. They do occur, and they will be found recorded by Politzer himself. Thus he says:—

"Lucae observed a rare case of primary cholesteatoma, in which the growth took its origin from the mucous membrane of the tympanic cavity, and in which there were no traces of a suppurative inflammation nor of a perforation of the membrane. Erdheim adds two more cases, in which there were absolutely no signs of immigration. Kuhn describes a case of primary cholesteatoma in a man, aged fifty-one years of age, who had suffered for one year from tinnitus, dizziness and hardness of hearing. This patient caught a cold, upon which suppurative inflammation of the middle ear developed with marked reactive symptoms,

great pain, and the formation of an abscess in the mastoid process." Operation revealed a large cholesteatoma which had exposed the lateral sinus and the dura of the posterior fossa. An instance of primary cholesteatoma infected not from the external meatus but through the Eustachian tube.

Cases like the last are probably less uncommon than is generally supposed. All operators have encountered acute otitis media, for instance, with mastoid symptoms in which operation surprises us by revealing the presence of cholesteatomatous material, usually in quite small quantity, in the antro-tympanum. Hitherto we have concluded, naturally enough, that this indicates a previous chronic suppuration overlooked by the patient. But, in view of the case just related, this conclusion requires revision.

Further, the possibility of an acute otitis media of nasopharyngeal origin infecting attic-aditus cholesteatoma even when it is small, must not be forgotten, since chronic suppuration may thereby be started. Such an accident, however, is doubtless rare, as in its early stages the cholesteatoma is closed, and when that is the case it will probably pass through an acute otitis media without becoming infected itself.

We have now reached the end of the second section of our inquiry, and I think it must be acknowledged that the view that aural cholesteatoma is always primary is one we can no longer ignore.

We may remark, by the way, that this opinion, although unpopular since Politzer promulgated the contrary teaching, has nevertheless always obtained the support of a number of authorities, of whom the first and greatest was Virchow.

The next step in our inquiry leads us to the consideration of the origin of primary cholesteatoma of the temporal bone. Is it possible that it is due to a developmental error?

CEREBROSPINAL CHOLESTEATOMA.—In this connection we may refer to a recent paper by Macdonald Critchley and Fergus R. Ferguson dealing with the cholesteatomatous tumours of the brain, in which the authors raise the question of the relationship of these growths to the aural cholesteatomata in general. The following points from their communication have an important bearing on the subject.

The intracranial cholesteatomata are rare tumours, arising most frequently in the subarachnoid cisternæ at the base of the brain. Formerly they were considered to be endotheliomata, but nowadays it is generally agreed that they are inclusion tumours formed by cells detached from the epidermis. It is suggested that their favourite sites—the cerebello-pontine angle is one of them, by the way—indicate some connection with the fœtal flexures of the central nervous system.

In appearance, and particularly in their microscopic features, they so closely resemble aural cholesteatoma when the latter is undisturbed by putrefactive changes, as to leave no doubt but that, whatever their respective origins may be, they are identical in structure.

Thus the authors say: "The [cerebrospinal] cholesteatoma is made up of an external epithelial membrane outside which there is a delicate fibrous tissue envelope. The interior of the tumour is composed of accumulated products of the desquamated epithelial layer."

In order to demonstrate the identity of structure of aural cholesteatoma and cerebrospinal cholesteatoma, I quote Critchley and Ferguson's clearly detailed description of the cell layer, known in these tumours as the *stratum granulosum*, but I shall use to illustrate their remarks a couple of figures from an article on aural cholesteatoma by Wyatt Wingrave. No device could more clearly display the structural identity of those two tumours. (Figs. 12 and 13.)

"The depths of the granular layer (our 'epidermal cell layer') vary with the specimen; in some instances it is only one or two cells in thickness; in others it may be built up of ten or more layers of cells which vary in character according to their depth. . . The typical cell is a

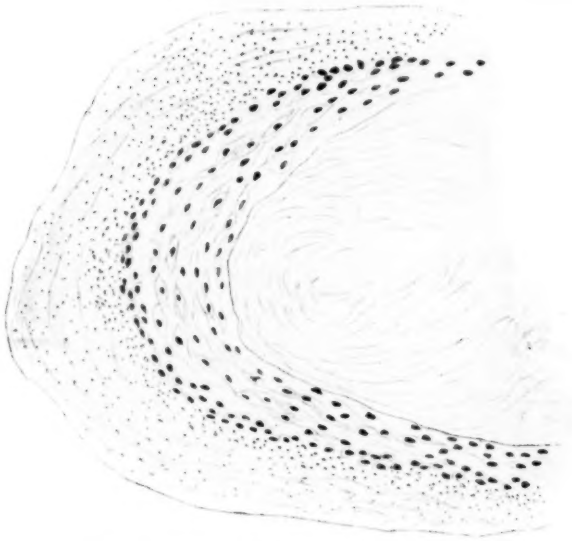


FIG. 12.—Aural cholesteatoma. Lining membrane.
(Milligan and Wingrave, "Dis. of Ear." By permission of Macmillan and Co.

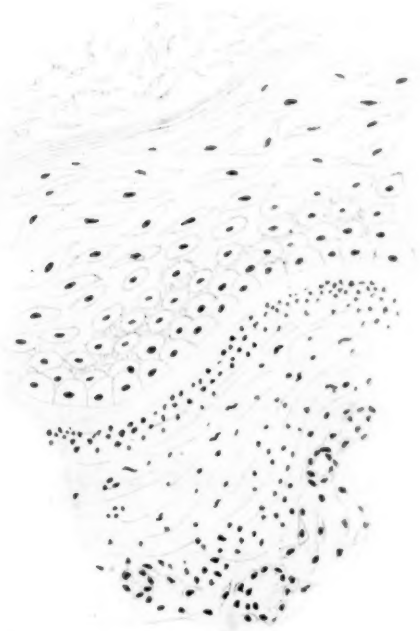


FIG. 13.—Aural cholesteatoma. Lining membrane.
(Milligan and Wingrave, "Dis. of Ear." By permission of Macmillan and Co.)

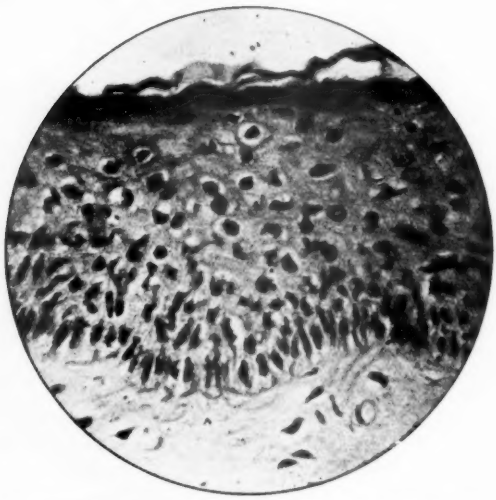


FIG. 14.—Epidermal layer of aural cholesteatoma showing palisade arrangement of deep cell layer. (H. P. photograph.)

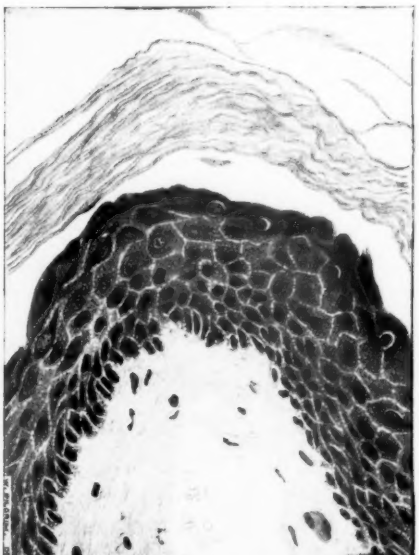


FIG. 15.—Cerebrospinal cholesteatoma; compare with fig. 17. (Critchley and Ferguson. By courtesy of the Editor of *Brain*.)

comparatively oval or circular structure with a large rounded nucleus. The cells are not packed tightly together, but clear, intercellular channels separate one from another '. . .' Fine granules composed of kerato-hyalin are scattered throughout the cytoplasm. '. . .' In the deeper layers . . . the granules become larger and more numerous."

"The morphological character of the component cells varies according to their depth. Immediately below the stratum durum" (our fibro-vascular layer) "the cells are oval and are arranged tangentially to those of the overlaying layer. A palisade formation may therefore result, provided that the section is cut in an accurately transverse direction." (Several of our sections show the palisade arrangement clearly (fig. 14)). "Below this layer is an intermediate zone of rounded cells; the apposition of one cell to another is loosest here, and the intercellular channels are clearly seen. There appears to be no definite cell arrangement. In the deepest layers the cells are more oval and are arranged with their long axes parallel with the stratum durum . . . granules here are very numerous." (Compare also with Critchley and Ferguson's fig. 15.)

Dr. Greenfield, I may add, to whom I showed our aural cholesteatoma sections, has no doubt of the two varieties being identical in nature and structure.

With fœtal inclusion tumours we are quite familiar in the instance of the dermoid. But the epidermoid (to which class these cholesteatomata of the brain belong) differs from the dermoid in that it contains only epidermal cells and their products. Dermoids are formed from more antique or primitive fœtal cells and contain mesoblastic structures; epidermoids are formed from cells which, being of late formation, are more specialized and show less variety; they contain no mesoblastic elements, not even blood-vessels. A few brain cholesteatomata have contained hairs. Have hairs ever been seen in aural cholesteatoma?

True epidermoids have also been found in the diploë of the cranial bones, and in their growth they erode bone.

PRIMARY AURAL CHOLESTEATOMA AN EPIDERMOID.—These data leave us with a strong suspicion that the admittedly primary cholesteatoma of the temporal bone, whatever may be its precise situation, is a real tumour, formed, like the intracranial cholesteatomata, by the inclusion during embryonic life of fœtal epidermal cells.

Further, if, as we have suggested, the so-called secondary cholesteatoma is merely a broken-up and infected primary cholesteatoma, then all the forms of aural cholesteatoma are, in like manner, epidermoids.

This conclusion may appear to be revolutionary. Nevertheless that it is worthy of serious consideration appears not only from the pathological relationship of aural with intracranial cholesteatoma, but also from certain clinical phenomena to which I am about to allude.

NEOPLASTIC FEATURES OF AURAL CHOLESTEATOMA. — In reading over Politzer's descriptions and arguments one cannot fail to observe that that writer is himself being influenced subconsciously by the feeling that in aural cholesteatoma he is dealing with a cell activity which is greater and more lively than that of its environment. As we have seen, he talks of the epidermis of certain parts as being "stronger" and "more prolific" than others. Kirchner, also, as we were careful to point out, looked upon the behaviour of cholesteatoma as reminiscent of a malignant growth. Now, although I have criticized the conclusions and have even doubted certain observations of these authorities, I agree with them concerning the clinical behaviour of the living cholesteatomatous cell. The process, described by Politzer, of feeble tympanic epithelium being elbowed aside or destroyed by cholesteatomatous epidermis is not the relationship of the normal, symbiotic cells of the body, but that of predatory and victim cells, inordinate "push" being, as we know, the hall-mark of the neoplasm.

That is to say, the cholesteatomatous cell in the ear behaves like a neoplastic cell. When, for instance, after a radical mastoid operation with a thorough curetting away of as much cholesteatomatous membrane as can be seen, several

FIG. 16.—Cerebrospinal cholesteatoma epidermoid (from section by Dr J. G. Greenfield). (A) Epidermal cell layer. (B) Lamellæ. (Drawing.)

FIG. 17.—Aural cholesteatoma showing: (A) Connective tissue layer; (B) Epidermal cell layer; (C) Lamellæ. (Drawing.) Compare with fig. 15.

months later there appears amidst a profuse overgrowth of exuberant granulations a tiny patch of white cholesteatoma, living and thriving in such adverse circumstances, the spectacle of its triumphant tenacity inevitably brings the fœtal cell to one's mind. It so closely resembles the dermoid and the thyro-lingual cyst, where every living epithelial cell has to be destroyed in order to obviate recurrence.

Now I find it difficult to credit ordinary epidermal cells with so great a vitality. We are acquainted with normal epidermis replacing destroyed epithelium but not with normal epidermis displacing normal epithelium—pushing it aside and taking its place. That is what Politzer claims for cholesteatoma, and he is quite right. But when he claims that power for the epidermis of the external auditory meatus as well, I think he is wrong. For, if our experience with the epidermis from the same external meatus when it grows to cover the granulations of the radical mastoid cavity, is any guide, its resisting power must be slight, since but a minor degree of septic infection is sufficient to destroy it. There is no such successful defiance in this instance as is seen in the patch of cholesteatoma flourishing in a swamp of granulations.

(I have sometimes wondered, by the way, whether those epitheliomata we occasionally find in these regions, in which the growth has made a surprisingly extensive invasion of the bone, are not due to an epitheliomatous transformation of a cholesteatoma.)

As another, if a minor point, favouring the epidermoid origin of aural cholesteatoma we may perhaps claim the frequency with which that disease manifests itself in the early decades of life, like the other congenital tumours.

OBJECTION TO THE EPIDERMOID THEORY.—But there is one fact that obstinately refuses to accommodate itself to this theory, and that is, that intracranial epidermoids are amongst the rarest of tumours, whereas aural cholesteatomata are quite common. True, were we to limit our claim to the equally rare primary cholesteatoma (we mean

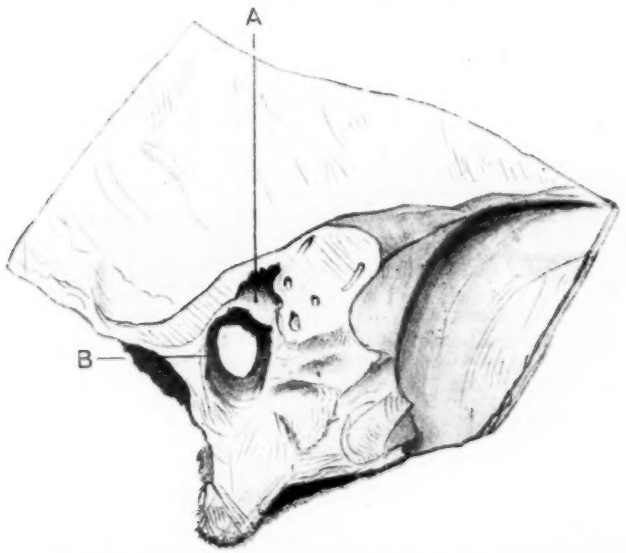


FIG. 18.—Temporal bone. The petrous has been removed to display the attic, aditus, antrum, and bony meatus from within. (A) Antero-inferior wall of antrum (the favourite site of cholesteatoma). (B) External auditory meatus.

here the " primary " of the orthodox school) our claim might be granted. But, as we are seeking the same origin for the ordinary aural cholesteatoma of everyday life, the difference in frequency calls for explanation. Is it possible to find the reason in the peculiar character of the neighbourhood of the postero-superior meatal fistula?

THE NEIGHBOURHOOD OF THE POSTERO-SUPERIOR FISTULA.—Let us examine a little more closely the situation and relationship of the postero-superior fistula region. The point is really one of importance to our inquiry. The region of the membrana and of the adjacent bone implicated in this perforation corresponds with the thin wedge of bone, measuring about 5 mm. square, that separates the cavity of the aditus-antrum from the external auditory meatus (fig. 18).

Viewed from the interior this area of bone will be seen to consist of the smooth anterior wall of the aditus just in front of the short process of the incus and above and a little behind the pyramid. At or about this spot lies the meeting place of the posterior limb of the annulus tympanicus, with the process of the squamous that comes down from above to close the open ring. And hereabouts also we have the junction of Shrapnell's membrane (which is merely a fold of fine meatal skin covering the ossicles) with the membrana vibrans. Thus the cholesteatoma, whatever its primal origin may be, most commonly appears in a small triangle that forms one of those developmental trysting-places (so to speak) where a frequent occurrence of inclusion cysts, arising out of cells detached from the primitive meatus during its formation, is only what we might expect.

By way of illustrating the tendency of the tympanic region to the formation of epidermal inclusions, I give here an illustration of a cholesteatomatous cyst of the membrana (fig. 19).

FIG. 19.—Cholesteatoma or inclusion cyst of left membrana tympani. (Drawing.) (See text.)

The patient was a man, aged 38; the small cyst lay at the umbo of the malleus. It was opened and curetted and was found to contain epidermal squames, cholesterin crystals and a few pus cells. It did not penetrate the membrane. The other ear presented signs of extensive cholesteatomatous disease.

SIMPLE SUPPURATION AND THE MARGINAL PERFORATION.—This is an appropriate moment at which to discuss an alternative view of the production of the marginal perforation, which we have so far glided over. We have seen how a primary cholesteatoma can erode its way through the bone of the meatus, and presumably its passage through the membrana would not present any difficulty.

But the question arises: Is the marginal perforation, or for that matter is the large perforation through Shrapnell's membrane which is perhaps the commonest of all cholesteatomatous sinuses, ever caused by simple suppuration, or does it always mean cholesteatoma and cholesteatoma only?

There is no doubt, of course, that small perforations through Shrapnell's membrane leading down to carious ossicles do exist without any sign of cholesteatoma. But what of the large open sinus, in which the whole or the greater part of the flaccid membrane is destroyed, and in which the free edge of bone of the attic-aditus wall is exposed, and perhaps rendered carious?

Now, as we know, in the more severe varieties of acute suppuration of the middle ear, both before and after the discharge through the membrana vibrans, inflammatory swelling of the posterior meatal wall is a common feature, significant of

the extension of the disease to the mastoid antrum. In such a condition we are obviously dealing with an attack upon the mucosa of the triangular wedge of thin bone we have just been discussing. Is it not possible therefore—nay, is it not probable—that, in some cases, osteitis of this plate may occur, abscess form and discharge, and with it or after it a certain amount of destruction of bone result, so giving rise to the typical attic or marginal perforation?

The importance of this little plate of bone, which seems rather to have escaped particular notice, has now become manifest.

On the other hand, however, if this event were to occur frequently, should we not come across instances in which small sequestra from this area of bone were voided in the aural discharges following acute suppuration of the middle ear? Yet sequestra of that sort do not appear.

Evolution of Primary Attic-Aditus Cholesteatoma.—We may suppose the following to summarize events in the development of cholesteatoma originating in this small chamber. We are assuming, of course, that it is beginning independent of suppuration.

Somewhere in the mucous lining, probably of the anterior wall, or at least anterior to and above the incus, a small collection of cholesteatomatous cells forms. The mass is spherical and cyst-like from the start. It proceeds to grow, and to distend the bony walls of the cavity. But, if favourably situated, while still quite small, it either makes its way through Shrapnell's membrane or it erodes the anterior bony wall of the aditus and more or less of the tympanic membrane. Then it discharges and dries up, and there is an end to it. Or infection of the exposed edge of the bone of the fistula takes place, granulations and polypi form, and we have chronic suppuration.

Or again, let us suppose that it is situated in such a position that easy access to the membrana and meatus is forbidden to it. (A small ledge of bone may suffice to alter its disposition and direction of increase.) Then, in its enlargement, it will grow up and back, until there is formed the typical cholesteatoma of the mastoid antrum, with that cavity distended into a relatively large excavation.

As we have already seen, the pressure-atrophy of bone may still go on after the meatal sinus has formed.

At any moment after cholesteatoma becomes infected it may lead on to infection of the normal tissues at the orifice of the fistula, in the attic, middle ear, mastoid or elsewhere, provided that they have been denuded of their cholesteatomatous covering, or are already devoid of it.

Why not Spontaneous Metaplasia?—As a final word, the possibility may be mentioned that, apart from developmental inclusion, the tympanic epithelium at this critical spot may have a natural tendency to be transformed into stratified squamous type. This idea appears, in reality, to be little more than a confession of ignorance. But we mention it for what it is worth.

The Cholesteatomatous Area of the Temporal Bone.—We are now in a position to delimit the region of the temporal bone in which cholesteatoma is most common. It comprises the attic, the aditus, the mastoid antrum, and the mastoid process, and in all of them cholesteatoma tends to open into the external auditory meatus. Moreover, the relative frequency of the disease would seem to follow the same order, being most common in the attic and least common in the mastoid process. (It may be noted that the attic and aditus frequently form but one cavity, the division of which into two is scarcely justifiable.)

Bearing on Treatment.—If the above sketch is true to nature, one important step in treatment is suggested, namely, in the case of disease limited to this small area and not getting well, to remove the thin plate of bone by punch forceps from the meatus so as to provide free exit for the contained débris. As the cholesteatomatous lining may be left *in situ*, if other symptoms indicative of wider infection are absent, the mastoid route of access is unnecessary.

Consideration of this aspect of our subject, however, raises a wider question. In the past, when dealing with cholesteatoma, the attention of the surgeon has been focused upon the supposed cause of the cholesteatoma, the suppuration of the middle ear, and his efforts have been applied to getting rid of this disease. But, as we have shown, middle-ear suppuration may be entirely absent. How many hearing ears have been destroyed by this unfortunate misconception?

CONCLUSION.—As a result of this inquiry, the chief conclusion I have come to is, that the supposed origin of cholesteatoma from suppuration of the middle ear is an error based upon a misreading of the clinical and pathological data. It was remarkable, to mention only one of the many surprises encountered in the investigation, to find how many odd clinical phenomena fitted each into its own appropriate niche, as soon as we had adopted the assumption that cholesteatoma was always primary.

With regard to the epidermoid theory I am favourable, but not so firmly convinced. Its chief attraction lies in its bringing aural cholesteatoma into close relationship with cerebrospinal cholesteatoma, and the cell activity seems to be highly significant, even impressive. At the same time, we must admit that the difference in frequency between the two types of growth is so far an obstacle to its whole-hearted acceptance.

ACKNOWLEDGMENTS.—In carrying out the work represented by this paper I have been fortunate in having been able to enlist the generous and kindly help of no fewer than five prominent pathologists. Of these, I should like to mention first Dr. Arnold Renshaw, of Manchester, since, from the inception of this investigation many years ago, he has undertaken the responsible and delicate work of preparing the necessary sections for the microscope. The result, as seen in the reproductions of his sections herewith, furnishes eloquent testimony to his expert skill.

In the matter of histological opinion, I have allowed myself to be guided by the wise counsel of Dr. G. Scott Williamson, Pathologist to the Central London Throat and Ear Hospital. I am also indebted to him for help in the reproduction of the sections.

To Dr. F. H. Teale I owe deliverance from an unfortunate accident that threatened us with the loss of our best slides. And to Dr. J. G. Greenfield, of the National Hospital for Paralysis, I am indebted for the loan of a slide of an epidermoid of the brain.

From Mr. R. J. Cann also, In-patient Registrar to the Central London Throat and Ear Hospital, I obtained a set of statistics showing the relative frequency of chronic suppuration of the middle ear over a number of years, as at one time I thought that they might have a bearing upon our theories.

Finally, my dear friend and respected teacher, Wyatt Wingrave, has generously placed his wide knowledge of a subject peculiarly his own at my full disposal, and as he was the first to arouse my interest in the problem of aural cholesteatoma it is but fitting that I should give his name the prominence of my final paragraph.

To one and all of these gentlemen I beg to offer my most sincere and grateful thanks.

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Discussion.—The PRESIDENT said that he had never been able to accept the theory that cholesteatomata had an embryonic origin, or that they were due to an invasion of the skin from the outer meatus.

In his opinion, the most tenable theory was that the process was dependent on some past sepsis—often not demonstrable—and that the irritant effect of this on the lining of the antral cavity and mastoid cells—which, as Neumann had pointed out, was a peculiar muco-periosteum—led to an accumulation of an abnormal desquamation.

These factors he suggested would be sufficient to account for such formations if associated with the one other factor required, a "bottle-neck" cavity.

Mr. CHARLES HEATH showed two cholesteatomata which he had removed from the external auditory meatus on each side of a patient, Miss R. T., nineteen years ago. There had been no suppuration, and after they were taken out a perforation was visible in Shrapnell's membrane on each side. He (the speaker) removed the patient's adenoids, and then both the perforations healed. He told the mother that he had not dealt directly with the area from which the cells came, and therefore did not feel certain that the end of the trouble had been reached, so that the patient must be seen by her doctor occasionally. Four months later she had acute mastoiditis in one ear; he operated by his conservative method, and the ear became well. Six months later she had a similar condition in the other ear; he operated again and that ear also became well. There was no loss of hearing on either side. He then told her he thought her ears were "safe," and that if she had otitis media again she had two safety-valves—one the drum, the other the membrane which closed the aditus. Only that week he had seen her again, after nineteen years, and she reported that five years ago she had influenza and otitis media on one side, the drum burst, and healed again in two or three days while she was in bed. Thus his forecast was verified.

The specimens which he was showing from this case were reported upon by Dr. Wyatt Wingrave as being true cholesteatomata, almost purely squamous cells. That endorsed what Dr. McKenzie had said, that sometimes there was no suppuration.

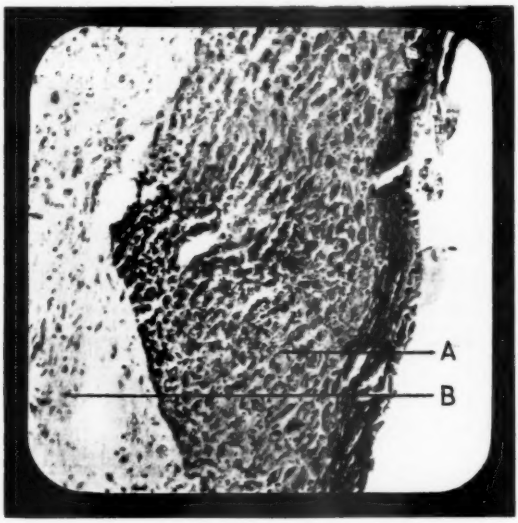
Miss R. T. Acute Mastoiditis: Material from Mastoid Antrum.

MATERIAL OF WHICH THE PATHOLOGICAL SPECIMEN WAS CONSIDERED TO BE COMPOSED.	REPORT BY DR. WINGRAVE (JANUARY 25, 1912).
A. (?) Fragment of bone and muco-periosteum of antrum.	*A.* Bone—acute leucocytic infiltration; muco periosteum—shows leucocytes, myelocytes, and many phagocytes, staphylococci well marked; indicates acute inflammation.
B. (?) Polypus blown out through perforation by air-bag and the writer's cannula.	*B.* Simply blood-clot.
C. Mass of cells and muco-periosteum from antrum. (?) Early cholesteatoma.	*C.* Pure cholesteatoma, cells devoid of nuclei, therefore not recent. Staphylococci very numerous.
D. Muco-periosteum from antrum.	*D.* Leucocytes and myelocytes well marked. Cholesteatomatous squames with active phagocytes containing staphylococci, which are numerous.
E. Cholesteatoma from meatus.	*E.* Pure cholesteatoma, staphylococci.
	REMARKS.—It is evidently an acute staphylococcal infection on a pre-existing cholesteatoma. Staphylococci are pure, no other bacteria. The bone is involved slightly, chief effects being apparently in the muco-periosteum, but that bone is active as shown by the large osteoblastic cells or myelocytes. The squames are not recent ones in the antral material, but some from the meatus are nucleated and therefore recent.

He (Mr. Heath) thought that the question as to where perforation took place had not been sufficiently dealt with by Dr. McKenzie. Perforations occurred where the discharge had access to the drum. In the later, i.e., the *acute* conditions, the two perforations were lower down. The discharge was able to get down to a part of the drum which was more easily penetrated, because the distribution of tympanic swelling allowed of it. Therefore the swelling of the mucosa was largely responsible for what happened to cholesteatomata produced in the antrum. He showed an illustration of a cholesteatoma from a case in which eight days after suppuration had set in, squamous cells began to appear. These rapidly increased in number, and as the deafness was increasing too, owing to increased swelling of

the tympanic mucosa, he had operated six days later. The photomicrograph, prepared by Dr. Wingrave, showed the squamous area in the mastoid antrum, which had been stimulated by suppuration from a double layer of squames, to twenty or thirty layers, showing that the process could not have been metaplasia; it was too rapid for that—it was the mere stimulation of an area which already produced squames.

In a large number of people part of the lining of the mastoid antrum was normally covered by squames, which could be stimulated into excessive reproduction and which, if the ciliated epithelium of the mucous membrane of the aditus were adequate, were passed along to the attic. In this case they were passing right through the ear to the Eustachian tube for a time; obviously, then, there was no obstruction. Later, obstruction occurred, and acute trouble followed. With such a squamous area in the antrum, and the distribution of the squames, guided by the locality of the attic swelling—which varied the drainage channel—we had the key to a large proportion of the early cases of cholesteatoma. One of his patients (shown) had had suppuration for four days, and cholesteatoma was found. It was



washed out through the perforation. Occasionally, when a cholesteatoma occurred, it was encysted, because the accumulation in the antrum had utilized the muco-periosteum as a cyst-bag to hold it. If there were much pressure, the bony antral irregularities would be smoothed out and the bag of cholesteatoma would approximate to a globular shape. This was not the commonest, or the earliest, form of cholesteatoma.

[Mr. Heath showed Two Recent Cases Illustrative of Cholesteatoma:—

(I) The first is still under treatment. In this case cholesteatoma had been found eighteen days after the onset of suppurative otitis media.

(II) In this case I visited the patient at Tooting Bec Hospital, only four days after the onset of otitis media. I immediately had her removed to the Downs Hospital, as I said her hearing was in great jeopardy. At the operation on both ears next morning cholesteatoma was found on both sides. When she was well enough to visit me I douched out the attic with bag and cannula; here in a bottle is the viscid material which I removed; it is cholesteatoma. The specimen shows how rapidly cholesteatoma scales may be developed and thrown off. The pathological report by Dr. Russ is as follows: "This material was blood-tinged and showed microscopically a small number of cholesterin crystals, amongst numerous pus cells. The epithelium was chiefly of the squamous type. There was also quite a lot of thick mucus

which gave the material a tenacious consistence. Bacteria were not very numerous and appeared to be mainly diplococci of the pneumococcal type."]

Mr. A. LOWNDES YATES said that he had been investigating the question of the cause of cholesteatoma and thought the condition must be divided into two categories, one in which the desquamation was due to the formation of an innocent epithelial tumour in the middle ear or mastoid, and to which the term cholesteatoma might properly be applied, and the other in which the condition was the result of desquamation of the epithelium of the middle ear or mastoid. He thought that the term cholesteatoma was incorrectly applied to this second class, for the ending "oma" suggested that the condition was due to the formation of a tumour.

He and his colleagues had first considered the question as to whether desquamation of the mucous membrane occurred during the process of inflammation of the middle-ear and found that even in cases in which there was no cholesteatoma, desquamated cells were not infrequently present in quantity in the discharge, and that a type of inflammation which caused such desquamation was produced more often by micro-organisms of the type of the streptococcus rather than by the staphylococcus. There was thus proof that there was desquamation from the mucous membrane in certain types of inflammation of the middle-ear. If there was obstruction to the escape of desquamated cells, this would collect behind the obstruction, and this had been cited by the President as the obstruction termed "a bottle-neck."

Desquamation might not collect in sheets within the ear as a result of inflammation, for in the similar process which occurred after scarlet fever, or in the type of eczema known as "washerwomen's hands," the desquamation did occur in sheets, in the first case as a result of infection with the streptococcus and, in the second, as a result of chronic soaking of the skin, both of which factors might be present in the middle ear. It did not therefore need a high flight of imagination to postulate desquamation in sheets from the infected mucosa, particularly when the inflammation was caused by micro-organisms of the streptococcal group.

The next question was the amount of discharge present in cases of cholesteatoma. He had found no cases in which a discharge from the ear was profuse and in which cholesteatoma was present; on the contrary, cases in which cholesteatoma had been found were almost universally characterized by scantiness of aural discharge.

The fact that dead micro-organisms or the mycelium of fungi were found in cholesteatomatous masses was a factor of importance, since such a collection, if formed of mycelium of fungi, might obstruct the escape of desquamated cells from the middle ear. He had seen cases in which the mass was chiefly formed of the mycelium of fungi in which the desquamated cells were already entangled.

Another factor which might have some bearing on the formation of cholesteatoma had also come out in this investigation, namely, that in the large majority of cases of cholesteatoma the pus was strongly alkaline, and that alkalies acting on the skin produced a desquamation. Atrophic rhinitis was another condition in which the pus was alkaline, and in that also there was microscopical evidence of a profuse desquamation from the mucous membrane. The reason of the alkalinity of the pus in these two examples of a somewhat similar inflammation had not yet been determined, and the question was whether it was due to the ferments liberated from the leucocytes when these died, or was elaborated by the micro-organisms? This question had been approached by treating small cholesteatomata, which appeared to be confined to the region of the attic, with dilute acid, when it was found that they rapidly disappeared, although no other treatment was afforded. One per cent. citric acid had been used in many cases for this purpose.

Mr. SYDNEY SCOTT said that he was in favour of the term "epidermoid" as used by Dr. Critchley and Dr. Ferguson in *Brain*.

[Mr. Scott described in detail a case met with in a patient who had no perforation of the tympanic membrane. The diagnosis was made by Dr. Jacobsen, of Aarhus, Denmark, when on a visit to St. Bartholomew's Hospital. Shrapnell's membrane was bulging, felt "boggy" and "pitted" when touched with Hunter Tod's probe. A few days later Mr. Scott operated on the mastoid and found the antrum, aditus, and attic occupied by ordinary cholesteatomatous material. There were no granulations and there was no pus.]

Mr. Scott said that this class of case lent support to Dr. McKenzie's contention. He himself, however, was more inclined to the theory of metaplasia, and felt sure that there must

be some preceding inflammation to account for the transition to the squamous epithelium. Mr. Lowndes Yates had described the growth of mycelium in cholesteatoma. He (the speaker) presumed that the fungus was a secondary invasion. He had certainly seen small cholesteatomata of the attic disappear after treatment with alcohol drops, and it had not recurred, but he had not ascertained whether there was a fungus in these cases.

[Mr. Scott showed Two Illustrative Cases :—

I. *Cholesteatoma with Destruction of Labyrinth.*—F. W., female, aged 27. Chronic otitis media, left side. First seen at St. Bartholomew's Hospital, June 23, 1930, when she complained of watering of the left eye (facial paralysis), and was sent to the Ear Department. She had a small perforation of Shrapnell's membrane, occupied by purulent cholesteatomatous material. She was absolutely deaf in the left ear in response to Bezold-Edelmann forks and the monochord—using Bárány's noise machine to control the right ear, which was normal. *Labyrinth tests*: No reaction to caloric or compression tests. No spontaneous or induced nystagmus.

At the operation, June 24, the whole of the bony labyrinth was found to be destroyed by cholesteatomata, which had accumulated to such an extent that the dura mater of both the middle and posterior cranial fossæ was exposed by the disease over an unbroken area, including the superior petrosal sinus. The cavity formed by the radical mastoid operation and by the removal of the cholesteatoma was much more considerable than a cavity formed by the radical mastoid operation alone. Fluid in the cavity transmitted pulsation from the brain. At one stage of the operation cerebrospinal fluid escaped, but the cavity was packed with "bipped" wicks, which were not completely withdrawn for over a week. The patient's recovery was not interrupted.

II. *Cholesteatoma with Fistula of the External Auditory Meatus and of the Labyrinth.*—J. H., male, aged 48. Chronic otitis media, left side. First seen at St. Bartholomew's Hospital in October, 1930, complaining of vertigo, which was worse when he inserted his finger into the left ear. He was in a frightened, apprehensive state of mind, which made an examination difficult. An attempt to syringe his ear to remove pus and débris terrified him, causing forced movements, so that he nearly fell off his chair. It was ascertained that nystagmus, with the primary movement of both eyeballs to the right—accompanied by forced turning of the head and face to his right when the left meatus was compressed. The same movements took place during the act of syringing the left ear. After removal of débris the tympanic membrane looked normal, and several observers failed to notice a fistula through the posterior superior wall of the bony meatus, which led into the antrum. A probe could be passed easily and painlessly through the fistula into the antrum without causing vertigo, unless it came into contact with the inner wall of the aditus. The violent forced movements, described above, were evoked every time the probe was applied to the same spot.

The hearing tests indicated only slight middle-ear deafness. The patient could hear Bezold's fork 24 d.v., but not 16 d.v. in the left ear. Two weeks after the extraction of the débris from the ear giddiness could not be produced by meatal compression, only by application of the probe to the region of the external semicircular canal.

The patient has ceased to be nervous and apprehensive, and expresses himself as feeling perfectly well, but will be kept under further observation.]

Sir JAMES DUNDAS-GRANT said that Dr. McKenzie's arguments had been very ably marshalled. Still, it was difficult to eradicate impressions, and he himself had been influenced by the teaching of Politzer, quoting Haberman and Bezold. The theory of epidermis having the mastery over the cells of the mucous membrane seemed acceptable, especially after what Dr. McKenzie had quoted concerning the extension of epidermis through a fistula communicating with a mucous surface. He showed on the screen an illustration of a frequent mode of formation of cholesteatoma in the attic. There was apparently an acute suppuration in the middle ear, covering almost all the tympanic membrane. On the screen was shown the bulging which had presented itself to him when the patient came to him with pain and evidently suppuration, in the middle ear. He incised that bulging, which obviously was from the attic, and after it had subsided and apparently dried up, it left a distinct dry cavity in the outer attic. This was the way in which, very often, cholesteatoma of the attic began and developed. He showed also a section of a portion of the tympanic membrane ; one could see the epithelium of the meatus and outer surface of the membrane extending through the perforation, and a commencing epidermization of the inner side. A section illustrated

showed a Malpighian layer, a nucleated layer, an un-nucleated layer, and detached layers of cornified cells, forming the contents and lining of the cholesteatoma. External cholesteatoma pure and simple was a very rare condition. He had had cases which caused him great trouble and anxiety, but in most of his cases he found that the cholesteatoma was continuous with a very deep cavity in the attic, and extending into the mastoid region. He considered that most of these cases were secondary proliferations into a cavity which had already existed.

An interesting case of cholesteatoma was one in which a boy who had acute suppuration was operated upon by Mr. Heath's method. The patient had now a perforation in the posterior meatal wall, and a cholesteatoma internal to it, which seemed to be a definite extension of the epithelium from the skin through the opening into the mastoid cells. The process was similar to that taking place in the healing of a flat ulcer, namely, a gradual epidermization of the cells extending over the granulations. It was practically necessary for the mucous membrane to have undergone some change, and if the surgeon could only enlarge the opening sufficiently, by chiselling away bone, or removing obstructions such as ossicles, or even a little band, a cure would ensue. He (Sir James) had had a very striking case under his care in which he had had to remove the lower margin of the attic, which formed a hammock by which the epidermic scales were kept from escaping. As soon as that "hammock" was taken away, the scene changed. The bottle-neck cavity was dealt with, and extraordinary improvement resulted.

Sometimes very mild treatment would produce the necessary result, and he thought tetrachloride of carbon formed a distinct addition to the otologist's armamentarium, as it cleansed a cholesteatomatous cavity very efficiently.

Kirchner said that cholesteatoma found its way into the canals of bone, but this was contradicted by Katz, and he, the speaker, thought that view was no longer held. In one case in which he had operated he had found, lying on the floor of the cavity, a white membrane, almost skin-like, as if it had been taken by a clever operator from the thigh and dexterously laid in the cavity. Fortunately, it was an incomplete but very suitable skin; if it had had hair follicles and sebaceous glands these would have caused great inconvenience.

Mr. MUSGRAVE WOODMAN said he would direct attention to two clinical points. Rhinologists knew of a condition in the nose in which ciliated membrane became transformed into a flattened epithelium, a condition which was difficult to get rid of. We had seen the advances which had been made by mild acid treatment, and in view of the leather-bottle shape of the mastoid cavity, the production of a cholesteatoma was easily understood.

The other clinical observation was with regard to the radical mastoid operation; it was a point to which Mr. Jenkins had drawn attention. The surgeon must remove all the ciliated mucous membrane lining the cavity. When he failed to do that, the little red carpet of ciliated mucous membrane travelled outwards to the many islands of squamous epithelium. When there was antagonism, the mucous membrane was the stronger of the two. He therefore subscribed to Dr. McKenzie's theory.

Mr. T. H. JUST said that within four weeks he had had two cases bearing on Dr. McKenzie's paper. One was in a man aged 26, who attended St. Bartholomew's Hospital, having, apparently, otitis media. He had had earache for sixteen days with a slight discharge, and some tenderness over the mastoid. There was no previous history of ear trouble. The drum was incised, and there was a discharge of sero-sanguineous fluid. The pulse-rate was 50, and there was well-marked papillœdema of 2 or 3 D. The patient became drowsy. The mastoid antrum was opened and a cholesteatoma about the size of a date-stone was found posterior to the antrum, in the tegmen region, and leading to thin bone in the middle fossa. On opening up the middle fossa he had immediately found a temporo-sphenoidal abscess. He did not know whether that was due to a previous suppuration, but the patient had had acute otitis media. The mastoid trouble cleared up after paracentesis, and behind it was the cholesteatoma.

In the second case the patient had come to the National Hospital for the Paralysed, practically unconscious, with pus coming from the right ear, and signs of a temporo-sphenoidal lesion. He was operated upon immediately. He (Mr. Just) did not see the drum. The meatus was filled with foul-smelling pus. When the pinna was pushed forwards the meatus was seen to be filled with cholesteatoma, and on investigation of the anterior wall of the mastoid, the posterior meatal wall, and also the cartilaginous wall, were found to be eroded. There was a large cholesteatoma which went mainly backwards to the posterior fossa. Though this was as large as a crown-piece, the dura was absolutely normal.

Upwards in the middle fossa the bone was partially eroded by cholesteatoma, and part of it was adherent to the dura mater. A small temporo-sphenoidal abscess was found, and also a large subdural abscess. The patient died. Dr. Greenfield removed the tympanum, and found an intact drum opposite the foul mass in the meatus. He (the speaker) did not know whether this patient had had previous sepsis or not, but there was a two years' history of intermittent discharge from the ear. He was sure that drum was not perforated during that time, though it might have been perforated previously. He had had a case of lateral sinus infection and septicæmia with a normal drum.

Mr. A. D. SHARP said he understood Dr. McKenzie to state that one did not find a "mushy" external cholesteatoma in the external form; he (the speaker) had seen a mushy cholesteatoma in both child and adult when there had been no perforation of the membrane.

Dr. T. B. JOBSON said that in treating suppurative otitis media by ionization one obtained an idea on this subject. He had tried to treat cases of cholesteatoma many times, but without any success. He had washed out the attic with ether and other substances but had failed to remove the cholesteatomatous mass, and cure the sepsis even when he had followed up this treatment by ionizing the cavity.

Chronicity did not explain this, because an ordinary case of otitis media might last ten or fifteen years and be efficiently treated with toilet measures—washing out and ionization—and success might come with only one ionization. That fact, he thought, corroborated Dr. McKenzie's contention that cholesteatoma was not a secondary condition due to suppuration but rather a primary condition on to which suppuration was secondarily grafted.

Mr. RITCHIE RODGER suggested that one argument in favour of the secondary origin of cholesteatoma was the fact that the condition was frequently bilateral, and bilateral otitis media and perforation were common, while a bilateral new growth was almost unknown.

Dr. DAN MCKENZIE (in reply) said that he sympathized with those Members who found it difficult to accept the views advanced in his paper; he had himself had to live with them fifteen years before he felt certain about them. The longer one lived with them the better one liked them. What were regarded as original ideas were too often merely resuscitated ones; those he had advanced to-day were the oldest of all.

Cholesteatoma performing for itself the Radical Mastoid Operation.—L. GRAHAM BROWN, F.R.C.S.

J. W., female, aged 45, complained of otorrhœa and deafness since childhood, following scarlet fever.

The right ear showed a large area of attic disease with the membrana tympani intact below. The left ear showed absence of the membrana tympani, granulations in the middle ear and a large loss of bony substance in the attic and the posterior wall of the meatus.

Operative treatment consisted in removing, through a posterior aural incision, a large mass of cholesteatomatous débris from the mastoid, antral and middle-ear regions, making a meatal flap, closing the posterior wound and draining through the meatus. The posterior wound healed completely in twelve days, but the cavity has not completely epidermized.

The hearing in this ear remains fair.

Congenital Deformity and Deafness.—E. BROUGHTON BARNES, F.R.C.S.Ed.

Patient, a boy, aged 9 years, has congenital deformity of pinna on both sides, and apparently some deformity of middle ear and ossicles; handles of both mallei appear scimitar-shaped. Severe middle-ear deafness. Absolute bone-conduction appears to be quite normal. The Eustachian tubes are patent.

Would removal of the membrane and ossicles help this patient?

The PRESIDENT said that this was a very important case. No one, he thought, would suggest immediate operation.

Section of Neurology, and Section of Ophthalmology.

[*November* 13, 1930.]

Chairman—Mr. LESLIE PATON, F.R.C.S. (President of the Section of Neurology).

DISCUSSION ON VASCULAR TUMOURS OF THE BRAIN AND SPINAL CORD.

Dr. Arvid Lindau (Lund, Sweden): Until quite recently, when dealing with cerebral growths the common term "brain tumour" was most used. This collective heading harbours a motley content, and is of little value, but research has now made it possible to deal with the nature, treatment and prognosis of the various tumour groups separately. In this way only can we compare the work of different investigators and the results of the neuro-surgeons.

The classification of Cushing and Bailey signifies a great advance, but it is necessary to take a further step, and the time now seems ripe to discuss the subdivision, made by Cushing and Bailey, of the vascular tumours of the brain and spinal cord.

These tumours are uncommon. In Cushing's extensive material they represent two per cent. of the histologically verified brain tumours; this figure would rise to three per cent. if several indubitable, though unverified, tumours of vascular origin were included. In Dandy's 600 cases of verified tumours those of vascular origin amount to five per cent. Recent publications on this subject are not rare. The closer knowledge of this kind of tumour is of great value for the neuro-surgeon, and their occurrence in certain systemic disorders throws light upon some hitherto obscure cases. For this reason the blood-vessel tumours of the brain have attracted more attention than their quantitative occurrence would justify.

In the past, vascular growths of the nervous system were all called angiomata, in spite of their varying character. Cushing and Bailey (1928) divided them into two major groups: (1) Angiomatous malformations and (2) the hæmangioblastomata or true neoplasms of blood-vessel elements, the latter being composed solely of mesodermal tissue, while the angiomatous malformations show their true character by the fact that traces of compressed nervous tissue are invariably present between the vascular loops comprising the lesion. This grouping is a great improvement as these two kinds of vascular growths differ in site, histological picture, and symptoms, and consequently require different treatment.

According to Cushing, the angiomatous malformations may be chiefly capillary (telangiectatic), chiefly venous (angioma venosum), or arteriovenous (angioma arteriale). Capillary telangiectatic malformations may occur in several parts of the brain—for instance, deep in the brain-stem. Usually they do not give rise to symptoms. The favoured site of the venous and arteriovenous angiomata is in the cerebral hemispheres; occasionally they are found in the hind-brain. Probably both the venous and the arteriovenous malformations are primarily meningeal or subpial lesions. In certain cases, however, the angiomatous growth extends with its apex towards the ventricle, with a terminal hæmorrhage as a not unusual complication. Only a small number of cases of this type has been subjected to histological examination. I take the opportunity to show a case observed by my countryman, Dr. Olivecrona. It is a mid-cerebellar angioma arteriale, in which the microscopic examination shows numerous wide blood-vessels, all separated by glial nervous tissue.

This type of superficial angiomatous malformation is met with both in the brain and spinal cord. Long ago, co-existing trigeminal nævi were reported, making a

clinical diagnosis of the nature of the brain lesion possible, and as regards the spinal cord, Stanley Cobb, Lhermitte and Cornil have noticed nævi about the trunk at the level of the medullary lesion. In the last few years a number of cases have been described in which, besides trigeminal nævi, homolateral pial angioma, showing calcification in skiagrams, and a unilateral buphthalmus (or glaucoma) together form a characteristic syndrome, often seen in young children, in a few cases (Kufs) with a family history. A hemilateral, local, vascular malformation of cavernous type, situated at the brain surface and in the skin, is evidently present. This cavernous angiomatosis of the brain and skin (called in France "syndrome neuro-cutané") is apparently quite different from the capillary angiomatosis of cerebellum and retina, described later.

I shall not discuss this cavernous angiomatosis of the brain and skin, as most of the research in that field has been done in this country by Dr. Parkes Weber and others, and a detailed survey from an ophthalmological point of view has recently been given by Dr. Ballantyne. I will only say that in Scandinavia similar cases have been observed, that Krabbe has published this year four cases, in which X-ray examination disclosed calcified meningeal angiomata, and that in three of these four cases the patients had nævi of the face, whereas no buphthalmus or glaucoma was present; all the patients were adults.

Now we pass to a discussion of the second of the major groups of vascular growths, namely, the lesions which are unmistakably neoplastic and composed of blood-vessel elements. Cushing and Bailey call them hemangioblastomata; in France they have been termed "angioréticulomes" by Roussy and Oberling; in my first publication the expression "angioplastic tumour" was used.

These tumours are not very rare. Besides the cases collected in Cushing's and Bailey's monograph, a number have been reported by Dandy, and in this country by Sargent, Greenfield and others. I have met with seventeen cases. As interest in these growths is of recent date, it would perhaps be wise to postpone the question of their frequency till more experience has been gained.

Their favourite site is in the cerebellum; sometimes they are met with in the medulla oblongata and the spinal cord; they have not as yet been found in the hemispheres. Their appearance to the naked eye may be vascular or not; often there is a certain yellow colour caused by the lipoid infiltration of the tumour. They may be compact, encapsulated lesions, but frequently they are more or less cystic. These cysts may be situated in the tumour itself or in its neighbourhood, and most commonly there is a single large cyst with a small mural nodule in the wall, as this slide (fig. 1) with schematic figures of four cases, shows. (The angiomata are dark and the boundaries of the cysts marked with the dotted line. A frontal section through the cerebellum in one of these cases [fig. 2] presents the cyst with the fluid fixed by formalin as a gelatinous content and with a tiny angioma embedded in the wall.)

Miscroscopically these growths usually show a sharp demarcation between the tumour and the nervous tissue. They are composed of blood-vessel elements with a more or less marked tendency to form vascular channels and spaces, but differ from ordinary capillary angiomata in having an abundant intercapillary tissue with swollen fat-laden endothelial cells. Thus we meet a structure known as hæmangio-endothelioma, and when the tumour is highly cellular and the capillary spaces are indistinct, a true diagnosis is not always easy; hence these tumours have been described in medical literature under a variety of names. Cushing and Bailey have called attention to the fact that in these cases Perdrau's silver nitrate stain reveals an elegant network of reticulum, peculiar to this kind of tumour, and showing that they are mesodermal in origin. A recent restudy of my own material has fully confirmed the great advantage of the Perdrau staining, as is clearly apparent from these slides (fig. 3).

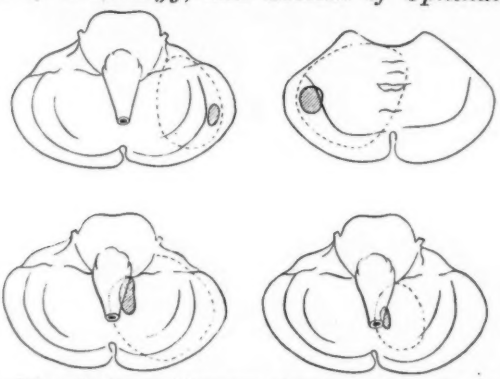


FIG. 1.—Schematic figures of four cases of cerebellar cysts with angiomata.

FIG. 2.—Angiomatous cyst with mural tumour.

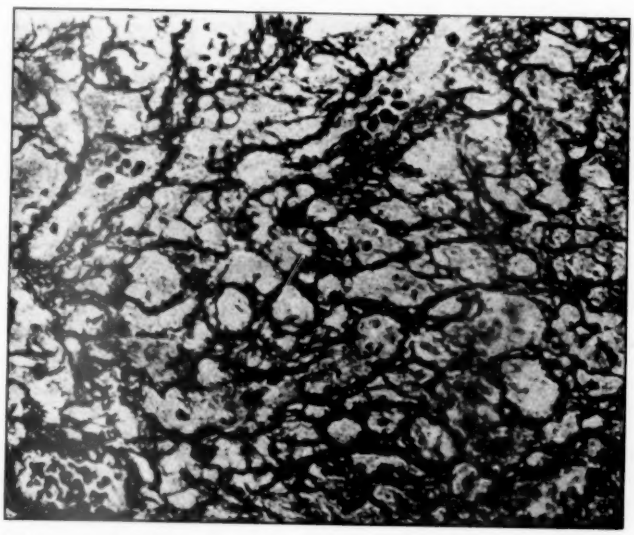


FIG. 3.—Microscopic picture of cerebellar angioma. Perdrau staining of the reticulum.

In most cases this intercapillary tissue is rich in fat-laden elements, called xanthomatous cells. This is apparently not a sign of degeneration but is to be ascribed to disturbances of circulation in the tumour tissue accompanied by stagnation of lymph rich in lipoids which are phagocyted by the endothelial tumour cells and thus transformed into foam cells.

Another striking feature is the tendency towards cyst formation. Microscopically there is a highly exudative power in these hæmangioblastomata marked by the emerging of a plasmatic transudate here and there in the tumour tissue. There may be smaller cysts in the growth itself, but more often the cyst is situated in the nervous tissue, adjacent to the tumour, and forms the far larger part of the lesion. The explanation is probably that the nervous tissue, owing to a lack of lymphatic vessels, cannot get rid of the fluid produced by the angioma, and thus a cyst is formed with walls consisting of compressed glia without an ependyma. That the mural tumour is the source of the fluid is clear from the fact that only operative excision of the growth keeps the cyst from refilling. Certainly the fluid of cysts with a glioma in the wall, another kind of cystic lesion rather like the angiomatous cysts, has the same vascular origin, and in this connection attention may be called to the fact that cerebellar tuberculomas, which are deficient in blood-vessels, never give rise to cyst formation. When the hæmangioblastomata are situated in the medulla oblongata or the spinal cord, the cyst formation only attains modest proportions, but occurs in most cases.

The hæmangioblastomata are most commonly solitary tumours, but not seldom there may be multiple cerebellar neoplasms or co-existing growths in the medulla oblongata or the spinal cord. This suggests a congenital anlage, and the microscopic picture which reveals the embryological type of the tumour cells points in the same direction. Thus Roussy and Oberling have found evidence of hæmopoiesis, a circumstance that Cushing and Bailey, as well as myself, have sought for in vain. A vascular anlage in or adjacent to the posterior end of the fourth ventricle (velum medullare posterior) may be regarded as the source of the hæmangioblastomata in the hind-brain. Here a rich capillary network is developed in the third fœtal month: later it takes part in the formation of the vascular plexus of the fourth ventricle and also forms the peculiar areas in the extreme posterior end of the ventricle, which are described by Wislocki and Putnam under the name of "areæ postremæ." At that point small circumscript hæmangioblastomata are occasionally present.

But the story of the hæmangioblastomata does not end here. The underlying early maldevelopment causing these tumours may also in certain cases give rise to a more general systemic disorder, a capillary angiomatosis of the central nervous system; besides the vascular growths in the hind-brain and the spinal cord, there may be angiomata of the retina and co-ordinated malformations or tumours in the somatic organs, such as a cystic pancreas, cysts of the kidneys, and hypernephromata of the kidneys or the suprarenal glands. These abdominal lesions never cause symptoms during life. They may be compared with the peculiar co-ordinated growths of the somatic organs found in tuberous sclerosis. These abdominal lesions, associated with capillary angiomatosis, are not vascular as far as I have observed. Thus the tumours of the kidneys or the suprarenal glands are of a benign hypernephroid type and the multiple cysts of the pancreas and the kidneys are not angiomatous. The cystic pancreas (fig. 4) is, in adults, almost pathognomonic for the syndrome.

The angiomata of the retina, long known by ophthalmologists under the name of v. Hippel's disease, offer far more interest clinically. The true nature of the lesion was first recognized by Treacher Collins in 1894. As an ophthalmological survey of this subject is also to be given, I shall not discuss the retinal angiomata at length, but shall concentrate upon the histopathology of these tumours. The explanation of the difficulties met by ophthalmologists in recognizing the nature of the lesion, is apparently the occurrence of secondary changes. The process slowly advances

during many years, with the formation of a reactive gliosis, proliferation of connective tissue, separation of the retina, and so on. All these secondary changes serve to conceal the nature of the primary lesion, making, as they do, a strong likeness to Coat's "exudative retinitis."

On account of this, the microscopic diagnosis is often rather difficult, and now and

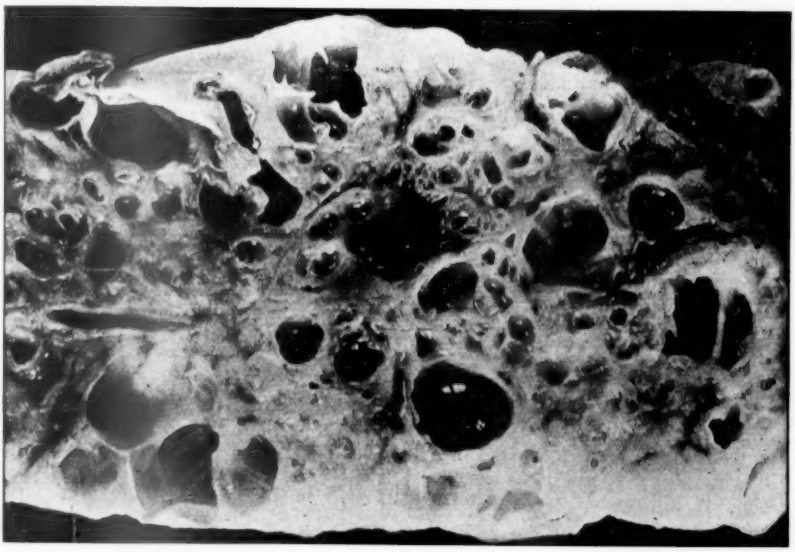


FIG. 4.—Cystic pancreas

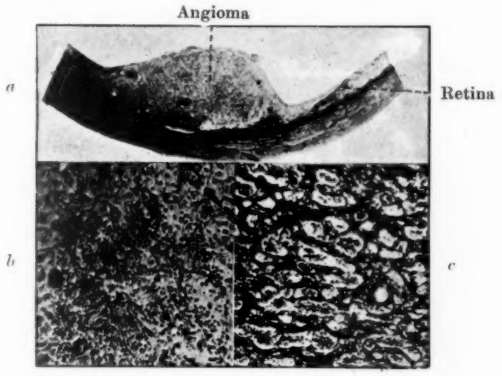


FIG. 5.—Retinal angioma. (*a*) Low magnification. (*b*) High magnification, ordinary staining. (*c*) High magnification, Perdrau staining.

then almost impossible; I can confirm this by experience from two cases of my own and from the examination of the eyes of about ten other cases of v. Hippel's disease. Recently I have tried Perdrau's stain on these eye lesions too, with the same good result as for the cerebellar hæmangioblastomata. Figs. 5 and 6 permit a comparison

between retinal angiomata stained by common methods and by Perdrau's silver impregnation. The diagnostic value of the latter method is high.

Only fresh cases without secondary changes can be of decisive importance for determining the nature of the lesion. Such cases have been described by Brandt, Wohlwill-Schuback and the speaker, and they all agree on the purely vascular character of the tumours. A primary "angiogliomatosis" cannot be found. Meller's and Marburg's recent paper does not alter this conception, as their interpretation of the case in question cannot be correct. This is shown by the pictures in the article and confirmed by a re-investigation of their slides by Dr. Percival Bailey. Thus, both microscopic examination and the co-incidental capillary angiomatosis of the cerebellum certify the vascular character of v. Hippel's disease. This correlation

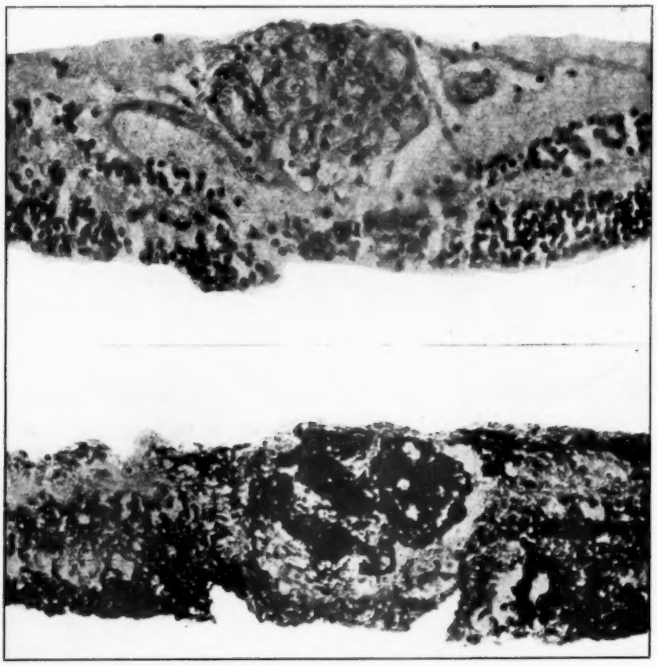


FIG. 6.—A tiny retinal angioma, ordinary staining (*a*) and Perdrau staining (*b*).

also explains why 25 per cent. of the cases of v. Hippel's disease give symptoms of a brain complication.

It is of great interest that the condition in about 20 per cent. of the cases has been found to be familial. Most pronounced are the two instances reported by Rochat and by Møller from Lundsgaard's clinic. In both these families the disease affects three generations.

In most cases there is no coincidental retinal lesion, and the cerebellar angiomata are solitary, just as the tumours of the acoustic nerve may be part of a general neurofibromatosis, but more often occur as solitary growths. A clinical pre-operative diagnosis of a cerebellar hæmangioblastoma is possible from the demonstration of a retinal angioma, or a family history, or both. Such were the circumstances

FIG. 7.—PEDIGREE. (H. C. Møller, *Acta Ophthalmologica*, Vol. vii, 1929.)

in Møller's beautiful case, the first, so far as I know, in which the pathological diagnosis was made before operation.

Dandy says of these tumours that surgically "they offer more than any other tumour of the brain." The excellent results of Cushing, Sargent, Dandy and others with patients observed for several years seem to show the possibility of a definite cure. But one must always keep in mind the possibility of the occurrence of a multiple lesion and the development of another angioma, as is probably the situation in Møller's case, which the first lesion was successfully operated on.

In rare cases the hæmangioblastomata have been situated in the spinal cord, usually producing cavities there. The cases of Tannenburg and Schuback seem to be true tubular gliomatosis co-ordinated with a vascular growth, while in the other cases the cavity formation corresponds to the genesis of the cerebellar cysts. On this account it would perhaps be wise to be restrained in using these cases in explaining the pathogenesis of syringomyelia.

Lastly I would only mention that in certain other brain tumours there is occasionally found an abundant vascular proliferation, which forms a great part of the lesion and must not be overlooked. For example there are gliomata often small and circumscript, where a coincidental disturbance and growth of both the blood-vessel elements and the glia are suspected. One would almost feel inclined to call these tumours "nævi glio-vasculosi." On the other hand Bailey has found that in rare cases the meningiomata may develop into growths of an angioplastic type. Further research in both these problems seems necessary.

In conclusion: I have adduced good evidence that the subdivision of the vascular growths into two major groups, angiomatous malformations and hemangioblastomata, has been well established and means a great improvement, both clinically and pathologically. Further I have shown that each of these groups includes a general systemic disorder, the first, a cavernous angiomatosis of the brain and the skin, associated with buphthalmus, but with no underlying angioma causing the eye lesion, and the second, a capillary angiomatosis of the cerebellum and the retina with coordinated characteristic lesions of the abdominal organs. Thus both these systemic disorders, although probably related and rather alike, clearly differ, and as we have never met with a coincidental occurrence of these two conditions in the same family, it would be better at the present stage not to mix them up with each other.

Sir Percy Sargent: It has long been known that the "blood-vessel tumours" of the central nervous system (leaving true aneurysms out of consideration), fall into two main groups: (1) Those composed obviously of blood-vessels, and (2) those which consist chiefly or wholly of angioblastic tissue. The grouping of these tumours under the names hæmangioma and hæmangioblastoma, although convenient for clinical purposes, should not, however, be too rigidly insisted upon. Not only are they related to one another, but they, doubtless, also have affinities with certain vascular gliomata and endotheliomata.

The masses of abnormal vessels which constitute tumours of the first group are usually spoken of as either arterial or venous, but both in their appearance to the naked eye, and microscopically, they are remarkably alike. It is very difficult to tell by inspection alone whether the vessels of which they are composed should be called arteries or veins; the walls are extremely thin, and they bleed with amazing ferocity when wounded. I think it is best to call such masses of vessels hæmangiomata without attempting to specify whether they are arterial or venous. They clearly belong to the pia-mater, and are usually superficial, although in some instances deep extensions have been noted. I have encountered in the operating theatre six cases of hæmangioma on the surface of the brain; in five the situation was either temporo-parietal or temporo-occipital, and in one it was cerebellar. In

the cerebellar case the condition disclosed by operation came as a complete surprise; in the others it had been suspected beforehand, either from clinical signs—such as audible bruit or variability of symptoms—or from the radiographic appearances of extremely vascular superjacent bone, such as we are familiar with in some cases of vascular endothelioma.

It is difficult to know what, if anything, should be done when such a mass of vessels is exposed. In two cases I did nothing, and the patients remained much as they were before operation, except that the headaches have gone. In four I ligatured many vessels, singly or *en masse*; some more or less temporary increase in paretic symptoms resulted in every case, and of the two in which an audible bruit was a prominent feature, only one was materially benefited. Subsequent ligation of the common and internal carotid arteries in one of these cases gave only temporary relief. The surgery of this particular class of case, has, therefore, in my experience, been very disappointing. All my patients are still alive, one after nearly ten years. It is said that these patients usually succumb to hæmorrhage from a ruptured vessel, and, indeed, when one realizes how thin are the vessel walls, and how furiously they bleed when wounded, it seems remarkable that a fatal termination is so long delayed.

Turning now to the somewhat similar condition found in the spinal cord, I have operated upon six cases, all in the lower thoracic or lumbosacral regions. By contrast with the cerebral cases, the vessels of the angiomata of the cord appeared always to be veins and not arteries. In regard to diagnosis, the clinical history may be of the utmost value, and the most striking feature is the remarkable manner in which the symptoms may vary from time to time.

In one of my cases the symptoms varied from day to day and sometimes even from hour to hour. The length of history during which "attacks" occur from which more or less complete recovery may take place is another striking feature. Thus, in a case recorded by Spiller and Frazier (*Arch. Neurol. and Psych.*, 1923, x, 29) there was a period of eight years between two "attacks" during which the patient was quite well. In another recorded case the history was spread over twenty-four years, and during this time there was a period of four years in which the patient was considerably improved. In one of my cases symptoms had been present for four years, and there had been several periods of well-marked improvement.

The cerebrospinal fluid was examined in three of my cases. In one it was of a golden-yellow colour and contained 0·6% of protein; in another it showed slight increase of globulin, with thirty small lymphocytes per c.mm.; in the third it was pale yellow, and contained 0·1% of protein with five cells per c.mm.

The characteristic variability of the symptoms makes it difficult to estimate the value of operative interference, and it is at least doubtful whether any real benefit was derived from operation in any of my cases. In so far as the symptoms may be due to compression, which may be assumed to vary from time to time with congestion or œdema, the decompressive effect secured by opening the theca and leaving it unsutured, may be beneficial; but it is clear that the symptoms are not wholly produced by mechanical pressure, and that they are more probably due to circulatory disturbances in the cord. Whether any attempt ought to be made to remove, or to cause thrombosis in the veins of the angioma I am not prepared to say, but the risks of serious injury to the circulation in the cord would seem to forbid any such procedure. The mere ligation of several of the veins, which I have practised, seems to be harmless, but ineffective.

I have also encountered a very curious case of a thrombosed aneurysm upon an artery of the pia-mater in which the clinical signs were those of a spinal tumour at the seventh cervical segmental level. An attempted laminectomy had to be abandoned on account of hæmorrhage, and at the post-mortem examination it was found that the cervical muscles, vertebræ and membranes were permeated by innumerable large arterial channels, the whole forming an immense plexiform angioma or cirsoid aneurysm. The vessels within the spinal cord were unaffected.

Hæmangioblastoma.—Cysts form about ten per cent. of all intra-cerebellar tumours. Examples of what are called simple serous cysts are to be found in many museums, but in the light of the cases which we are now considering it is at least probable that some of these are in reality cysts connected with tiny hæmangioblastomata which have escaped observation. Virchow described a cyst which had a demonstrable communication with the fourth ventricle, and he regarded it as a developmental ventricular anomaly; easily explained by the manner in which the cerebellum is developed. Doubtless, too, parasitic cysts are sometimes found.

But the majority of cerebellar cysts are connected with either gliomata or simple hæmangioblastomata, and it is probable that the latter are at least twice as common as the former. The recognition of such cases is no new experience, and I will give a brief abstract of an early observation of the greatest interest.

> A healthy girl, 20 years of age, attended the London Hospital with a history of failing vision for three months. It was recorded that her sister, who had had two previous fits, died in a seizure without regaining consciousness. There was also a clear account of a severe head injury sustained by the patient herself seven years previously. On examination what was called double-optic neuritis was present, and the vision gradually deteriorated while the patient was under observation, until she became totally blind. It was noted that there was no defect of co-ordination, no weakness of the limbs or nystagmus, and it is recorded that: "The most striking clinical feature of this case was the remarkable intermission of the symptoms." The patient died suddenly, and the account of the post-mortem examination states that there was in the right cerebellar lobe a smooth-walled cyst one inch by one inch and a half in diameter containing clear, serous, yellowish fluid. In its outer wall was a tumour, the size of a shilling, which, on section, showed a firm, yellowish centre, merging into adjoining highly vascular parts. The outer portion of this tumour reached the surface of the cerebellum immediately under the pia-mater.

I have taken this account from *The Medical Times and Gazette* of 1872, and the case was reported by Hughlings Jackson. It is to be noted that he had observed nearly all the points which characterize these cases, and on which a diagnosis may sometimes be made before operation, as was done in two of the cases which I have just shown. There is first the suggestive family history, then the history of antecedent injury, and then the observations as to the mildness and variability of the focal symptoms, despite the evidence of increasing intracranial pressure. I have operated upon four such cases within the last few years. In the first two the tumours were removed at second operations: in the last two the diagnosis was made beforehand, the cyst was deliberately explored and the tumour removed. All four patients are alive and well.

Mr. E. Treacher Collins: OCULAR HÆMANGIOMATOUS FORMATIONS ASSOCIATED WITH VASCULAR TUMOURS OF THE BRAIN AND SPINAL CORD.—Ocular hæmangiomatous formations, presumably congenital in origin, occur in connection with both the retinal and the ciliary vessels. Cushing and Bailey [1] in discussing new growths connected with the blood-vessels of the brain, divide them into two classes:—(I) Those composed of fully formed blood-vessels, which they say scarcely deserve to be regarded as tumours, and term "angiomatous formations." (II) Those composed of the cellular elements of blood-vessels, which they say may without equivocation be regarded as neoplastic, and be appropriately called "angioblastomata."

A similar division may be made in the growths occurring in connection with the retinal blood-vessels. First there are cases in which fully formed retinal vessels are unusually tortuous, or branch abnormally, a condition accompanied by little, if any disturbance of vision and which remains unchanged for an indefinite time. To such a condition some hesitation might at first be felt in applying the term angioma,

were it not that it is often associated with undoubted angiomatous formations in the skin and mucous membrane, and sometimes with symptoms suggesting tumour formation of an angiomatous character, pressing on the cerebrum.

Entirely distinct from this class is that in which an immensely enlarged retinal artery and vein lead to and from a raised mass in the periphery of the fundus, composed of rudimentary capillary blood-vessels and inter-capillary endothelial cells, with, sometimes, cystic formations. Lindau has shown that these cases may be associated with similar vascular and cystic growths in the cerebellum.

Retinal angiomata or tortuous fully-formed retinal vessels.—Several cases of tortuosity of the retinal vessels have been recorded. The first, however, which I have found described in connection with head symptoms is published in the Clinical Society's *Transactions* for 1879 by Dr. W. Allen Sturge [2] under the title: "A case of partial epilepsy apparently due to a lesion of one of the vasomotor centres of the brain." A description of the condition of the eyes is given by Nettleship. The case was that of a girl, aged 6½, with an extensive "birth-mark" of a deep purple colour, on the right side of the head and face, extending as low as the third or fourth dorsal vertebra behind, and to the second costal cartilage in front. The lips, gums, tongue, and roof of the mouth, were all similarly affected to a greater or less extent. All the affected parts were larger than the corresponding parts on the opposite side. The right eye was larger than the left, being myopic whilst the left was hypermetropic. All the visible vessels on the surface of the right eye were larger than those on the left, whilst downwards and inwards in the front part of the ciliary region was an ill-defined purplish or lilac patch in the sclerotic. Ophthalmoscopically the right optic disc was seen to be much redder than the left, and the right upper retinal veins were very tortuous. The general colour of the choroid was darker and redder than in the left, suggesting venous capillary hypertrophy.

Six months after birth this child began to have fits of twitching in the left side of the face, arm and leg, lasting about ten minutes. When eighteen months old she began to lose consciousness during the fits, which became convulsive commencing with a "funny feeling" in the hand. Dr. Sturge attributed the fits to some vascular development on the surface of the right side of the brain similar to that present in the skin, mucous membrane and retina.

In 1882, Benson [3] and Nettleship [4] each recorded a case of tortuosity of the retinal blood-vessels unassociated with any hæmangiomatous affection of the skin or any history of head symptoms. In the following year a case, very similar to that of Dr. Sturge's, was described by Dr. Horrocks [5], also with a note as to the eye condition by Nettleship. It was that of a girl, aged 9, the right side of whose face, including the skin of the eyelids and forehead, was the seat of a port-wine-coloured nævus. The right eye showed a network of enlarged anterior ciliary veins over the sclerotic on each side of the cornea. The retinal veins in this eye were exceedingly tortuous, contrasting strongly with those of the other eye which presented a normal appearance. Since birth the girl had been subject to epileptic fits, often two or three in a day, causing clonic spasms of the left side of the trunk and limbs. She was hemiplegic on the left side, the left arm being in a permanent state of flexion and rigidity. Dr. Horrocks suggested that possibly the blood-vessels of the pia-mater on the right side of the brain were affected and were the cause of the fits.

Dr. Stephen Mackenzie [6], in 1884, reported three cases of tortuosity of the retinal veins. In one of them, that of a woman aged 20, the main trunks of the retinal veins in her left eye were slightly dilated and twisted, being coiled round in places in a corkscrew-like manner, a few of the smallest arteries were also a little tortuous. In her right eye the retinal vessels were normal. She had a high degree of hypermetropic astigmatism and a convergent strabismus. She complained of much pain on the left side of the head, of a throbbing, shooting character, from which she was

never entirely free. Heurtelouping and the administration of bromide of potassium gave her no relief.

Work Dodd [7], in 1901, recorded the case of a woman medical student with nævi in the middle portion of the upper lip, in the middle of the right upper lid, in the left popliteal space, and a cicatricial condition of the skin, in the left fronto-temporal region, left by vaccination at the site of a former nævus, several large veins being still present. The retinal vessels in the left eye—both arteries and veins—were remarkably tortuous but there were no abnormal anastomoses.

Hartridge [8], in 1901, described the case of a woman, aged 25, with a nævus of the eyelid and face and what he spoke of as a nævoid condition of the vessels of the optic disc, affecting chiefly the veins.

These cases serve to show that tortuosity of the retinal blood-vessels, apart from any apparent neoplasm in the eye, may or may not be associated with hæmangiomatous formations in the skin, and at times occur in connection with symptoms indicating pressure on the cerebrum, probably due to some similar intercranial formation. The ophthalmoscopic recognition of tortuous retinal blood-vessels might, therefore, in a case presenting symptoms of cerebral tumour, aid in a preoperative diagnosis, just as the presence of a retinal angioblastoma has been shown by Lindau and Cushing to aid in the preoperative diagnosis of the nature of a cerebellar tumour.

Angiomata of the mucous membranes may also be associated with tortuosity of the retinal blood-vessels. In 1917 I showed at a meeting of the Ophthalmological Society [9] a man aged 57, whom I had had under observation for six years. On the optic disc in the left eye, were several remarkably tortuous veins, the main retinal vessels running a straight and normal course. In the skin of his left lower eyelid were two separate vascular nævi each about the size of a large pin's head. In the skin of his left temporal region he had a large mottled capillary nævus. Since boyhood he had been liable to attacks of bleeding from the nose, the blood coming mostly from the left nostril. On examination of the nose, a small patch of dilated veins was seen on the left side of the septum. I remarked, when I showed this case, that the association of recurrent epistaxis, due to a nævus of the nasal mucous membrane, with an angiomatous condition of the retinal blood-vessels, suggested a possible explanation of the cases of recurrent epistaxis in young men associated with recurrent attacks of hæmorrhage into the vitreous humour, to account for which no adequate cause has so far been found. Cases of this description were first described in a paper by Henry Eales [41] in 1881 in which he says:

> "In all of my own cases the calibre of the retinal vessels was unusually large in both eyes, the veins especially being dark, large and tortuous. In two of my cases the retinal veins at the periphery were found to present remarkably corkscrew-like tortuosities."

Jonathan Hutchinson [42], who also recorded several cases of this description, says that "If we can find the usual cause of epistaxis at any given age, we shall have found the cause of the intra-ocular bleeding also."

Retinal capillary angiomata or retinal angioblastomata.—The value of pathological research in the elucidation of clinical phenomena and the development of treatment is well shown in the upgrowth of our knowledge in connection with the retinal angioblastomata. As already stated, this form of new growth presents distinctive ophthalmoscopic characteristics, familiarity with which readily leads to its diagnosis.

The first account of the clinical appearances of the affection were described and pictured by Fuchs [11] in 1882, under the title of "An arterio-venous aneurysm." Much increased attention has been attracted to it since the publication of Lindau's thesis on "Cysts of the Cerebellum" in 1926, in which he showed that retinal angioblastomata may be associated with similar formations of a cystic nature in the cerebellum, spinal cord, pancreas and kidneys.

Some sixty or seventy cases of retinal angioblastomata have now been recorded and careful reviews of them have from time to time been published, by Coats [12] in 1908, by Cushing and Bailey [13] in 1928, and by Paton and Williamson-Noble [14] last year. It is unnecessary for me to repeat what has been there summarized, and I propose to confine my remarks on the subject mainly to the pathology of the affection, which raises several interesting points for discussion.

My attention was first drawn to this affection when, as pathologist at the Moorfields Hospital in 1893, I came to examine the eye of a man, John M., aged 20, blind, owing to detachment of the retina, which, shortly before its removal, had become glaucomatous and painful. He had been exhibited at the Ophthalmological Society the previous year by Dr. D. J. Wood [15], and a drawing of the ophthalmoscopical appearances of his other (right) eye was published in the *Transactions*. Its vision was then reduced to six twenty-fourths, and there was a detachment of the outer part of the retina, with enormous dilatation of the blood-vessels passing to it; the vessels passing to the undetached inner part of the retina remaining unaltered. In the detached part of the retina were several irregularly-shaped patches of hæmorrhage, and in the undetached part, besides numerous small white dots, a large white patch over which the retinal vessels coursed. The first symptom of failure of sight in this patient's left eye had been noticed six months previous to its removal.

Shortly after I received for examination the two eyes of this patient's sister, Julia M., who was six years his senior. She had had good sight up to the age of 10 or 11, when it began to gradually fail in both eyes, and at the age of 12 she was quite blind. In 1892 when she first came to the hospital, both corneæ were enlarged, opaque and staphylomatous. She could not tell light from dark, and the eyeballs were exceedingly painful and tender. Both eyes were excised at the same time, their removal being accompanied by considerable hæmorrhage.

I thus had the opportunity of examining pathologically three eyeballs presenting different stages of what was evidently a familial affection, resulting in rapid and complete destruction of sight. The familial tendency of the disease has been amply demonstrated in recent years by Rochat [16] and Møller [17], who have each published pedigrees of three generations, in which members were affected, some with angioma of the retina and some with angioma of the cerebellum.

I [18] published a description of my pathological findings in these three eyes in the *Transactions of the Ophthalmological Society* for 1894. In all I discovered a growth composed of a plexus of thin-walled capillary blood-vessels, which I located as having begun in the retina, some of the main blood-vessels of which were enormously dilated and thickened. In places the growth had undergone cystic formation, and in the sister's eyes it was mainly due to the formation of cysts in their interior that the eyeballs had become enlarged and staphylomatous. In her eyes also there had been some invasion or absorption of surrounding tissues, such as the lens, iris and cornea.

Lying between the capillary vessels of the growth I found some cells presenting an unusual appearance, of which I published a drawing, but of the nature of which I was at the time unaware. These cells had large nuclei and their cytoplasar appeared to be mapped out in a sort of honeycomb fashion. Similar intervasculm cells have since been described by other observers in connection with cerebellar angioblastomata. Lindau compared these cells to those of the xanthomata, and accordingly speaks of them as "pseudoxanthoma zellen." Some writers have described them as "neuroglial cells of epithelial aspect," but Cushing and Bailey have shown that they contain a large amount of fat in the form of small droplets, and that when this fat is dissolved out in the process of embedding, the honeycomb appearance of the cytoplasm is produced. They say that "By careful study of the tumours it is easy to follow the transformation of the endothelial cells of the capillary network into the swollen, fat-laden intervascular cells."

It is important to recognize that these angioblastomata are neoplasms of mesoblastic tissue growing in a neuro-epiblastic structure, and that in this respect they differ from the so-called gliomatous growths of the retina, in which also there is a new formation of blood-vessels, but which are neoplasms of neural epiblastic tissue with mesoblastic vascular accessories.

In the angioblastomata the capillary vascular formation is the predominant factor, the intervascular endothelial proliferation being a secondary feature. Neoplasms are, however, met with in which the intervascular endothelial proliferation preponderates over the vascular formation, a form of growth which is termed a hæmangio-endothelioma. I have met with [19] and recorded in the *Transactions of the Ophthalmological Society* for 1892 one case of a new growth of the retina, which should I think be so classed. The tubular character which such growths present histologically necessarily renders their differentiation from gliomata a matter of some difficulty. The age-incidence of these two forms of growth is, however, very different; the case I described occurred in a woman aged 65 years, a time of life at which glioma of the retina has never been met with. One of the three cases recorded by Brant [20] in 1921, in which the growth was cellular rather than capillary, appears to have been of a similar type. It did not manifest any clinical symptoms until the third decade of the patient's life.

In these hæmangio-endotheliomata, in which the cellular element is the predominating characteristic, there is a probability of malignant tendencies becoming manifest and of metastatic growths being formed. It would be interesting to know if some of the cerebellar tumours of a more solid than cystic character are not of this nature.

The fact that the retinal arteries are "end-arteries" (the main divisions into which the arteria centralis breaks up forming no inter-anastomosing capillary network) accounts for the characteristic ophthalmoscopic appearance which an angioblastoma presents, viz., that of an isolated swollen area in the periphery of the retina in which a much dilated companion artery and vein terminate. The case of a woman, aged 20, recorded by Foster Moore [22] in 1912, in which angioblastomata are shown in the retina, uncomplicated by any sequelæ, demonstrates well how the new growth is situated at the site normally occupied by the capillaries between an artery and vein. This patient had also recurrent attacks of nose bleeding, for which, however, a rhinological examination revealed no cause.

Though in some cases only one swollen area is present and one companion artery and vein are dilated, it has been shown by v. Hippel and Paton that in cases watched over a long period fresh balloon-like swellings may develop in different parts of the fundus, the vessels leading to them becoming enlarged and tortuous. Such observations throw doubt on the congenital nature of these growths, but Lindau has recorded the presence of an angioblastoma in the retina of microscopic size which would escape detection ophthalmoscopically.

In the *Transactions of the Ophthalmological Society* for 1918, I [23] published a drawing of the fundus of the right eye of a woman, aged 26, who had been under my care for six years. It showed multiple swollen areas in the peripheral parts of the retina with dilated vessels terminating in them. The left eye had vision of $\frac{6}{9}$, but there was in that eye also a swollen area in the retina, connected with the inferior temporal vessels. I saw this patient again ten years later; she was then blind in both eyes, and told me that her sight had failed completely in the course of a few months after the drawing had been made. For some years she had had recurrent attacks of pain in the eyes; these, however, had ceased during the previous year. There was then complete cataract in each eye; the pupils were inactive and there was one posterior synechia in the right eye, in which the tension was slightly increased, that of the left eye being normal. Her general health at that time seemed good and she made no complaint of any head symptoms, but I heard

that she died three months later from what was stated to be meningitis. She was one of a family of three; one of her brothers, killed during the war, had been "cross-eyed," but apart from this there was no history of any eye affection in her family.

The clinical history of the eye affection in this case, which I had watched over a period of seventeen years, corresponds with that of two, described by v. Hippel [24], which he had watched, for nine years and five and a half years respectively, the vision in both of which slowly deteriorated, and in which there were repeated hæmorrhages, detachment of the retinæ, signs of iritis and secondary cataract.

The detachment of the retina in these cases is mainly due to cystic formation in angiomatous growth. Cystic formations are very common in atrophic retinæ in which the nerve elements have disappeared and the neuroglial framework has become spaced out by albuminous exudate. The cystic formations in these eyes with angiomatous growths seem, however, to be of a different character, and to resemble those which occur in angiomatous growths in the cerebellum, the question as to the pathogenesis of which has been fully discussed both by Lindau and by Cushing and Bailey. These writers favour the view that the cysts are due to active transudation of lymph from the vessels of the growth rather than to a mere replacement by fluid of an area of degeneration. In both the eyes of the woman, Julia Martin, which had become staphylomatous, I found the interior occupied by large cysts, from which straw-coloured fluid escaped, and which had smooth walls containing nodules of vascular growth, which were no doubt the source of the fluid contents.

In 1911 v. Hippel described the pathological examination of an eye excised for secondary glaucoma sixteen years after the onset of the disease; he found the interior of the globe lined by a tumour-like mass, consisting exclusively of coils of vessels supported by neuroglial tissue, which he described as much proliferated in places. In one place he found that a large retinal artery had acquired a connection with the choroidal vessels, which were gigantically enlarged, but neither in this case, nor in any other which I have found recorded, was there the extensive invasion of the front of the eye by the vascular growth, and the formation of the anterior staphylomatous condition of the eyeball present in both eyes of the woman Julia Martin, which I described in 1894.

That a growth composed of thin-walled capillary blood-vessels should give rise to recurrent hæmorrhages is only what might be expected. When such a growth is situated in the retina, the blood effused would collect in the tissue of the retina; or—after breaking through the internal limiting membrane—in the vitreous chamber; or, after breaking through the external limiting membrane—between the retina and choroid. Recently effused blood has been seen ophthalmoscopically in the tissue of the retina and in the vitreous chamber in cases of retinal angioblastomata. In the latter situation newly developed blood-vessels often extend into the coagulum which is formed, and fibrous tissue develops in it, a condition somewhat inappropriately spoken of as "retinitis proliferans" being produced. The contraction of such fibrous bands, which are adherent to the retina, is another factor which tends to bring about its detachment. Blood which collects and coagulates between the retina and choroid may, as I was able to demonstrate very definitely in a case I recently recorded, have new vessels from the retinal blood-vessels growing into it. Fibroblasts are formed, the clot then being replaced by fibrous tissue of almost cicatricial consistency, cholesterin crystals, or the spaces in which such crystals have formed, frequently being found in it. Such a sub-retinal formation of fibrous tissue is the condition which I think Coats somewhat unfortunately spoke of as "massive exudation." Ophthalmoscopically it gives rise to the appearance of dense white plaques in the fundus, sometimes raised above the level of the surrounding parts, but always situated beneath the retinal blood-vessels, which course over it.

These white plaques, due to fibrous tissue formation in sub-retinal blood-clots, are met with not only in connection with retinal angioblastomata, but also in connection with other cases in which the blood-vessels are diseased, so that hæmorrhage may take place from them, as, indeed, was very clearly shown by Coats.

Another kind of membrane, which is produced in connection with intra-ocular angiomatous growths which have existed for some time, is of a fibro-osteogenetic character, and appears to be an effort on the part of the surrounding mesoblastic tissue to encapsule the growth. Such a fibro-osteogenetic membrane was present, external to the vascular growth, in both the eyes of Julia Martin, and also in the case of retinal angioblastoma examined pathologically by v. Hippel. As I shall show later, fibro-osteogenetic membranes are also found in cases of choroidal angioma. So far as I know no such membranes have been found in connection with cerebellar angiomatous cysts, but they have been demonstrated as present by X-ray examination in connection with angiomatous growths above the tentorium in the cerebrum.

When a cystic angiomatous growth of the cerebellum has been diagnosed it is possible, as shown by Hans Ulrik Møller, for it to be removed successfully and the patient's life be saved. When, however, the retina is affected by a similar growth, blindness always ensues, the eye often becoming glaucomatous and painful, so that it has to be removed. The question naturally arises: If a case is seen in an early stage of the affection can nothing be tried to arrest its progress? Ejler Holm, in two cases, applied radium treatment to the eye and by it witnessed diminution in the growth. Two years ago I suggested the possibility of treating the affection by electrolysis, but have not, so far, had the opportunity of putting it to the test. An electrolysis needle, well insulated up to its point, might, I suggest, be passed through the coats of the eye into the growth, in order to produce coagulation of the blood in it, the current being turned on immediately the needle entered the growth to avoid extravasation of blood into the vitreous. The exact spot at which to insert the needle so as to enter the growth could be determined by the ingenious technique devised by Gonin for ascertaining the position of a hole in a detached retina.

Angiomata of the Ciliary Blood-vessels.—Angiomata occur in connection with both the anterior and posterior ciliary blood-vessels.

Angiomata of the Choroid.—The first adequately described cases of choroidal angiomata were published in the *Transactions of the Ophthalmological Society* by Jennings Milles [25] in 1884 and by J. B. Lawford [26] in 1885. In 1919 our Chairman, Mr. Leslie Paton, and myself [27] recorded a case in a boy aged 14, in which we diagnosed the probable presence of such a growth in an eye with detachment of the retina and secondary glaucoma, from the presence of a large vascular nævus on his cheek and round the margin of the orbit on the affected side. We were then able to collect the records of fifteen cases. Though the affection is a rare one, several others have since been published. That the disease is probably congenital in origin is borne out by the fact that defect of sight has been noted in some cases as dating from birth; it has not been, however, until about the end of the first decade of life, or later, that symptoms have arisen necessitating removal of the eye, so that the nature of the growth could be confirmed pathologically. In Wagenmann's [28] case the eye was not excised until the age of 50. Apparently all cases ultimately end with detachment of the retina and secondary glaucoma. A large vascular nævus affecting the skin of the face on the same side as the eye involved was present in about half the cases.

Nettleship, in Sturge's case already referred to, diagnosed the presence of an angioma in the choroid ophthalmoscopically, from the darker and redder colour which it presented compared with that of the fellow eye, and also from its association with tortuous retinal blood-vessels, and a vascular nævus of the skin of the face on

the affected side. Its presence, however, was not confirmed by pathological examination. The ophthalmoscopic appearances of an angioma of the choroid which was so examined is recorded by Fehr [29] in a case which he was able to watch for 20 years before the eye was removed. The patient complained at first of a cloud over his left eye, and on examination there was found to be a central scotoma and contraction of the field of vision to 30°. In the region of the macula a small greyish-white flat swelling was seen with, in places, a rough glistening surface. Its upper and lower edges were dark, as in a pigmented sarcoma. A retinal fold stretched between the optic nerve and this swelling, and there was a definite detachment of the lower part of the retina. The sight of the eye slowly deteriorated and in ten years was reduced to counting fingers at one foot.

In a case recorded by Meller [30] the patient suffered from intense photophobia previous to the loss of sight from detachment of the retina, a symptom which Meller attributed to twitching of the retina caused by varying degrees of engorgement of the growth.

I have had the opportunity of examining microscopical sections of three specimens of choroidal angiomata (Milles', Lawford's, and Paton's). In all three the growth was situated in the posterior part of the choroid and was of the nature of a cavernous angioma. Irregularly shaped spaces, containing blood, were separated from one another by walls composed of strands of delicate fibrous tissue lined by endothelial cells. In some recorded cases these boundary walls have tended to be more cellular than in others. Cases in which the cellular elements of an embryonic type were a predominating feature of the growth would have to be classed with those which Kerchbaumer has grouped as perivascular hæmangiomata or perivascular endotheliomata, and which possess malignant characteristics.

The most interesting feature respecting the choroidal angiomata from a neurological point of view is their tendency to become encapsuled on their inner surface by a fibro-osteogenic membrane, and this quite apart from any inflammatory reaction. In Milles' specimen there is a connective-tissue layer on the inner surface of the growth, containing a small hard plate exactly resembling an early stage in the formation of bone. In Lawford's case the fibrous tissue formation on the inner surface of the growth is very small in extent and confined to the vicinity of the optic nerve. In Paton's specimen an extensive covering of fibrous tissue containing plates of bone had developed on the inner surface of the vascular growth and some of the bony plates completely encircling the innermost vascular spaces. Tailor mentions the presence of fibrous-tissue formation on the inner surface of the growth in his case, and Nordenson [31], Wagenmann [28], Steffens [32] and Fehr the presence of fibrous osseous plaques in theirs.

The formation of these fibro-osteogenetic encapsuling membranes in connection with intra-ocular angiomata may, I suggest, be compared with the membranes shown radiologically around long-standing cerebral angiomata. Parkes Weber [38] in 1922 was the first to demonstrate by an X-ray examination of the head the presence of what he took to be a calcified membrane around an old unilateral hæmangioma.

The case was that of a woman, aged 28, with right-sided spastic hemiplegia of congenital or early infantile origin, congenital hæmangiomatous nævus of the left side of the face, and a blind left eye from buphthalmos. Shortly afterwards observations of a similar nature were recorded in the Argentine. These are referred to by Cushing and Bailey in their book on "Tumours arising from the Blood-vessels of the Brain" as follows:—

> "Three remarkable examples of congenital facial nævi associated with epilepsy and in each of which a calcified lesion was radiographically disclosed in the occipital lobe have been reported from the Argentine, the first of them by Dimitri (1924) and the other by Marque (1927). The patients were all children of 13.6 and 10 years respectively at the time calcification was first observed."

It will be noticed that these writers, as the result of their radiological observations, speak of *calcified* membranes in connection with these angiomatous formations, whereas the membranes I have found in connection with the intra-ocular angiomata have been *ossified*. It will be interesting to know if pathological examination does not reveal the presence of bone in the intracranial membranes also.

Angioma of the anterior ciliary vessels.—Angiomata of the iris, due to the situation of that structure in the front part of the eye, would, it might be thought, be easily recognized. A few recorded cases in which there was a protuberance of the iris, from which blood exuded and collected in the anterior chamber, have been so diagnosed, but the diagnosis has not been satisfactorily substantiated by histological examination. The best recorded case of angiomata of the iris is one recently described by Arnold Knapp [33], in which a pathological examination of a piece of the iris, which he had removed at a trephining operation for the relief of increased tension, was examined by Verhoeff. The case was that of a boy, aged 11, who had a diffuse vascular nævus of the skin of the face, upper extremities and trunk, and also of the gums and hard palate. There was nothing very distinctive in the appearance of this clinically to suggest the presence of an angiomatous growth. It was described as "off-colour," of a dull greyish-blue. On its surface there was a network of superficial branching white lines, and some dilated vessels were visible. The most striking feature in the iris was the presence of many greyish nodules scattered over it without any zone of predilection. Both eyes were involved and both had become glaucomatous, with deep cupping and atrophy of the optic discs. Each eye was trephined at the upper limbus, and it was noticed that on dissecting down the conjunctiva an unusual plexus of episcleral vessels was exposed. Microscopical examination of the piece of iris removed showed it to be thickened owing to proliferation of endothelial cells with many new-formed blood-vessels. The nodules on the surface of the iris were composed of cells crowded together in layers.

In this case the condition then appears to have been an angiomatous growth of the iris in which an increase of the peri-endothelium was one of its most conspicuous features. Though an increase in the size of the episcleral vessels had not been noted in the first place, an unusual plexus of them was exposed on dissecting down the conjunctiva. In several other cases in which there was a cutaneous vascular nævus of the eyelids and face, enlargement of the episcleral and ocular conjunctival blood-vessels has been noted. In Sturge's case, referred to at the beginning of this paper, Nettleship spoke of an ill-defined purplish or lilac patch in the sclerotic in the ciliary region, which he termed a "scleral nævus." In Horrocks' case Nettleship also described an enlarged network of the anterior ciliary veins.

Yamanaka [34] in 1927 collected the records of fourteen cases in which a cutaneous vascular nævus was associated with glaucoma. Waardenburgh [35], at the International Congress at Amsterdam last year, stated that "nævus flamens of the face, and also frequently of several other parts of the body, was described about thirty times in connection with glaucoma, mostly hydrophthalmos." The glaucoma in these cases is usually unilateral, but bilateral cases have been described. When unilateral, the nævoid condition of the skin and the glaucoma are always on the same side, showing an intimate association between them.

When increased tension of an eye begins early in life, while its external coat is still elastic and expansile, the whole eyeball becomes enlarged, the condition described as "buphthalmos" or "hydrophthalmos" being produced.

Safar [36] examined pathologically an eye with hydrophthalmos which was associated with a vascular nævus of the face, and attributed the increased tension to abnormalities about the angle of the anterior chamber, viz., incomplete development of the canal of Schlemm and of the scleral spur, with thickening of the iris tissue at the angle of the anterior chamber. These findings are similar to what I and other investigators have described as commonly met with in cases of hydrophthalmos. I have shown that the extent of the malformation at the angle of the anterior

chamber varies considerably in different cases, the time of onset and degree of increased tension of the eye varying accordingly.

In 1906 Harvey Cushing [37] in a paper entitled "Cases of Spontaneous Intracranial Hæmorrhage associated with Trigeminal Nævi," described three cases of extensive vascular nævi of the skin on one side of the face with buphthalmos on the same side, and contralateral epileptic symptoms which he attributed to intracranial hæmorrhage from a vascular growth.

In 1929 Parkes Weber [39] was able to collect eight cases in which buphthalmos was associated with cutaneous and cerebral (not cerebellar) hæmangiomatosis, and suggested that whilst retinal hæmangiomatosis was most likely to be associated with disease (cystic angioma) below the tentorium cerebelli (Lindau's syndrome), buphthalmos was associated with hæmangiomatosis above the tentorium.

From the material here put together I think I may add that tortuosity of fully-formed retinal vessels is also at times associated with hæmangiomatosis above the tentorium cerebelli. Further, that though angioblastomata or true vascular tumours of the retina are associated with growths of a similar character in the cerebellum, no case has, so far, been recorded in which they have been found associated with hæmangiomatosis above the tentorium cerebelli.

Lindau believes that angioblastomata do not occur in the cerebrum, and Cushing and Bailey say that they have not themselves met with one so situated. From their examination of the literature of the subject they conclude that "the list of true blood-vessel tumours of the cerebrum is an exceedingly meagre one."

Angioblastomata in both the retina and the cerebellum are mesoblastic new-growths situated in an epiblastic environment, but as to why they show this predilection for the tissue of the small rather than the large brain no explanation has as yet been given.

Though all forms of intra-ocular angiomata are liable to result in secondary glaucoma, it is only glaucoma which dates from birth or very early life which causes buphthalmos: such a glaucoma, e.g., as is due to a primary congenital malformation at the angle of the anterior chamber obstructing the exit of the intra-ocular fluid.

In conclusion, it has been shown by a case recently recorded by Foster Moore [40], that intracranial hæmangiomatosis may give rise to ocular symptoms quite apart from any new formation in the eyes themselves. It may, like any other intracranial new growth, give rise to papillœdema by causing increased intracranial pressure; or give rise to homonymous hemianopsia by involvement of the visual cortex.

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Since the above article was written one covering somewhat the same ground has been published in the "British Journal of Ophthalmology" for October, by A. J. Ballantyne.

Dr. J. G. Greenfield: In our interest in the fascinating combination of anomalies to which Dr. Lindau has introduced us, we are apt to forget the relationship of these discoveries to general pathology. From textbooks on pathology we learn that capillary hæmangiomata are tumours or malformations of congenital origin; that they usually grow little if at all during life, but that they may take on a habit of progressive growth and invade surrounding tissues or, since they are mesoblastic tumours, may become sarcomatous. There is evidence that the tumours of the retina and cerebellum have the same characteristics. The familial history, the presence of more than one tumour of the same kind in a patient, or the association of one or more of these tumours with other abnormalities, such as those which Dr. Lindau has described in the pancreas and kidney, indicate their congenital nature. In several of my own ten cases of capillary angioma the tumours associated with cerebellar cysts have been extremely small; four of them have been smaller than a pea. And as the symptoms were entirely due to the cyst formation there was no evidence that the actual tumour was enlarging. Sir Percy Sargent and I have recently brought forward evidence that trauma may start the cyst formation when a small tumour is already in existence. In the history of three of our cases blows on the head occurred shortly before the onset of symptoms. In Seidel's case and in one of Cushing's cases the same definite association with trauma is found. If, therefore, some of these capillary angiomas do not grow, or grow only very slowly, there seems little justification for the use of the word "hæmangioblastoma" as a generic name for them.

The possibility that they may become sarcomatous is suggested by the case recently published by Sladden in which the tumour in the eye, removed twenty years before death, was so cellular that it was impossible to classify it definitely as an angioma. Sladden considered, however, that the absence of mitotic figures was against the diagnosis of sarcoma. There were also in this case true capillary angiomas in both cerebellar hemispheres and in the left kidney. This appears to be the only case in the literature in which capillary angiomas of the kidney were found in association with cerebellar tumours of the same nature.

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Dr. George Riddoch: I will confine my remarks to some of the features of the clinical picture of intracranial hæmangioblastomata.

Those tumours are clearly congenital, but they seldom give rise to symptoms before the second, third or fourth decade of life. It would appear that solid tumours declare themselves at an earlier age than cystic ones. In Cushing's collection of solid tumours the average age was 24½ years, while in Dandy's series it was 25 years, though that series included a baby aged one month. Two of my own patients were 24 and 20 years old respectively at the time of onset of symptoms. In the cystic variety, however, the average age of the two series (Cushing's and Dandy's) was 39 and 35½ years respectively. The ages of my own two patients were 43 and 42 respectively. Cystic tumours appeared to be much more common than the solid ones.

Once disorders of function have begun to develop, the course tends to be more rapid with cystic than with non-cystic tumours, and the interval between the onset of the headache and of cerebellar symptoms, with the possible exception of giddiness, is shorter with the cystic variety, probably because the cyst grows the more rapidly.

The clinical picture begins with paroxysmal headache, which occurs on waking or is brought on by stooping, coughing or sneezing. The attacks may be long or short. The pain, which is sub-occipital, frontal, temporal or general, is described as aching or shooting. It may be associated with vomiting with or without nausea, but this may be late in appearing, as for example in one patient who did not begin to vomit until fifteen months after the onset of headache. These bouts of headache, between which the patient may for months be perfectly well, are undoubtedly due to intermittent hydrocephalus. It is to the intermittency and briefness of the attacks of hydrocephalus in the earlier stages of the complaint that the prolonged absence of papillœdema must be attributed. The optic discs may be normal for months (eighteen months in one patient) after headache has commenced. (In none of the speaker's patients was angioma of the retina found.) This long interval between the onset of paroxysmal headache of the hydrocephalic type, and papillœdema, is one of the striking features in the clinical picture. In time, hydrocephalus, of course, becomes persistent, with the usual results. The attacks of headache are more prolonged, papillœdema develops, along with diplopia, from sixth nerve palsy, and mental dullness. In association with severe headache consciousness may be temporarily lost and "tonic" fits develop.

Another interesting point in the clinical story is the delay in appearance of prominent cerebellar symptoms and signs. Giddiness, it is true, may occur simultaneously with headache, but it may not be noticed for a year or longer afterwards. It is, however, distinct from the giddiness of hydrocephalic attacks, for it is provoked by movement of the head and is independent of the headaches. Apart from giddy attacks, the first indications of cerebellar disorder are a stiff attitude of the head, unsteadiness in walking and turning, and slight hypotonia, with clumsiness of the fingers, usually unilateral, or more on one side than the other. Unsteadiness in walking had developed sufficiently to arrest the patient's attention eight months and fourteen months in two cases of cystic hæmangioblastoma, and three and a half years in a case of non-cystic tumour in the fourth ventricle, after the onset of headache. Nystagmus at this stage is commonly absent and dysmetria is often slight.

Interesting extracerebellar focal signs, due probably to pressure on the bulb and posterior column nuclei, were described by Cushing and Bailey, and were present in one of the speaker's cases. They consist of unilateral or bilateral defective postural sensibility in the fingers and toes, and astereognosis. Tingling and numbness may also occur, as well as an extensor plantar response on one or both sides. These abnormalities are not, however, peculiar to cerebellar hæmangioblastomas, for they may develop with other tumours or cysts in this situation.

Reviewing the clinical picture, which has been only briefly sketched, it is suggested that a presumptive diagnosis of the nature of the tumour can be made at the bedside, even in the absence of a retinal angioma. The diagnostic points on which I would lay stress are the age at which these tumours commonly begin to produce symptoms, the long history of intermittent headaches of the hydrocephalic type, the late appearance of papillœdema and cerebellar signs, and, if present, a retinal angioma.

Dr. Dorothy Russell: It has been pointed out by Lindau and others that the true capillary hæmangiomata, or hæmangioblastomata, appear to be confined to the subtentorial parts of the central nervous system. Above the tentorium these tumours are of doubtful occurrence. On the other hand, two distinct kinds of vascular tumour are found in the cerebral hemispheres—using the word tumour in a wide sense: first the cirsoid aneurysms, and secondly the cavernous hæmangiomata. The structure of these cavernous tumours has been little studied

by recent workers, and my observations will be principally concerned with this group.

In the Institute of Pathology at the London Hospital there are records of nineteen cases in which blood-vessel tumours have occurred in the central nervous system. They are divided into cirsoid aneurysms (seven cases), capillary hæmangiomata (four cases), multiple capillary telangiectases (one case) and cavernous hæmangiomata (seven cases).

The cirsoid aneurysms appear to be angiomatous malformations of congenital origin. They are composed of abnormal arteries and veins. Their site of origin is in the leptomeninges, and they involve the underlying brain secondarily by extension. It is not proposed to discuss these further.

The first of our four cases of true capillary hæmangioma is of interest historically, as the second example of Lindau's disease to be recorded chronologically. It was reported by Turner (1888) in the *Transactions of the Pathological Society of London* as a case of cystic growths in the cerebellum and right adrenal. There were also cysts in the kidney and liver. In the fourth case a capillary hæmangioma of the cervical enlargement is associated with syringomyelia extending upwards to the medulla and downwards to the tenth thoracic segment. There are two histological features in this specimen to be emphasized in connection with the discussion that follows: first, there is no capsule separating the capillary loops from the surrounding nerve tissue and, secondly, tongues of glia extend into the tumour for considerable distances. The greater part of the interstitial tissue is, however, composed of fine reticulum which is clearly demonstrated by Laidlaw's silver method.

Our single case of multiple capillary telangiectases should, strictly speaking, be included with the angiomatous malformations. It has to be considered, however, as a possible precursor of the cavernous hæmangiomata. In these telangiectases groups of greatly dilated capillaries are seen, the individual loops being separated by nerve tissue.

The cavernous hæmangiomata usually occur above the tentorium, and occupy either the white matter of the hemispheres or the basal ganglia. They appear each as a lobulated or mulberry-like mass, which, on section, presents a congeries of small and large spaces containing blood, or blood-clot, the blood spaces being separated by a mesh of grey fibrous strands. They have no anatomical connection with the meninges and are not, in our series, associated with cyst-formation.

Microscopically, they consist essentially of a non-encapsulated system of cavernous and capillary spaces the walls of which are wholly composed of collagen and are lined with a single layer of endothelial cells. For the most part these walls are thin and indistinguishable from those of capillaries. They are, however, very frequently thickened by reduplication of the collagen and then it often appears that the walls of adjacent blood spaces have coalesced. This is commonly seen in the central parts of the tumour and in these areas a variable amount of reticulum is demonstrable while glia is absent. In some instances the amount of reticulum that can be demonstrated is comparable with that seen in the true capillary hæmangioblastomas. There is, however, no endothelial proliferation in the interstitial tissue in these cases such as is found in the hæmangioblastomas, and the absence of this feature may be of importance in separating these two types of tumour. The blood spaces in the outlying parts of the cavernous hæmangiomata are usually separated by nerve tissue in which a conspicuous gliosis is demonstrable.

It is difficult to decide whether these cavernous tumours are to be regarded as angiomatous malformations or as true neoplasms. The nature of the interstitial tissue has been used as a diagnostic criterion by Bailey and Cushing. They have suggested that reticulum is the characteristic interstitial element in the true

tumours, or hæmangioblastomata, whereas glia is found always between the vessels in the angiomatous malformations. Their series of cases did not, however, include any of the kind under present discussion. If their criterion is rigidly maintained it would be necessary, I believe, to include many cavernous hæmangiomata amongst the true neoplasms. It may be found, however, that the presence or absence of endothelial proliferation in the meshes of the reticulum is a more trustworthy guide. On the other hand, it may be argued that the cavernous hæmangiomata are closely allied to the capillary telangiectases and are derived from them by fusion of adjacent capillary loops.

The relationship of these cavernous hæmangiomata to Lindau's disease also has to be considered, in view of the fact that lesions of the Lindau syndrome type were found in other parts of the body in two of our seven cases. In one of these, multiple cavernous hæmangiomata of the central nervous system were associated with a blending together of the suprarenal and renal cortex on the left side. There were many small cysts in this suprarenal and in the adjoining kidney and, in addition, there were several capillary telangiectases in the medulla of the same kidney. In a second case a solitary cavernous tumour of the cerebrum was associated with a capillary hæmangioma of the subcutis of the buttock. This skin lesion, however, was of a telangiectatic rather than of a neoplastic character.

Whether they are regarded as neoplasms or as angiomatous malformations there seems little doubt that these cavernous tumours form a distinct group, being separable on the one hand from the subtentorial capillary hæmangioblastomata, and, on the other hand, from the meningeal cirsoid aneurysms. Their possible connection with Lindau's disease will be an interesting point for future inquiry.

Mr. L. B. Rawling said that his own experience of the conditions under discussion had only extended to three or four cases.

In 1923 he had seen a boy, aged 5 years, who was supposed to be suffering from a cerebral tumour. There were attacks of headache and vomiting, but no papillœdema or other visual change was present. There was, however, a marked outward bulging of the bone in the frontal region. This region was trephined there, and on opening the dura mater a sero-sanguineous discharge was evident, and beneath that, over the whole area exposed, was a large tortuous mass of veins, greatly engorged in appearance, and of the type which, as Sir Percy Sargent has pointed out, one was anxious to avoid injuring. He (the speaker) had sewn up the wound, and from that time onwards the boy was relieved of his headaches and had no more fits. In 1928 he was in St. Bartholomew's Hospital with an enormous hæmatoma on the right side of the face, through rupture of some veins and the escape of blood through the osseous and dural aperture. So, by reason of a decompression over the angioma, one would alleviate headache, etc., at the expense, however, of an external hæmatomata. The hæmatomata subsided, and the boy is now quite well, though there is some bulging over the right frontal region.

Three years ago a radiologist had shown him (the speaker) a skiagram of a boy, aged 7 years, who, ever since birth, had been troubled with weakness on the left side of the body and also had had fits of various kinds. There was a very large angioma occupying the right half of the face, in the distribution of the first and second divisions of fifth nerve. On X-ray examination, an extraordinary angiomatous condition, with calcified vessels, was seen occupying the right half of the cerebrum, more especially in the occipital region, whilst the subtentorial region was quite clear. On antero-posterior section it could be seen that the condition extended deeply into the brain substance. It was important to lay stress on the fact that these angiomata were seldom confined to the surface—they almost always extended deeply into the substance. In one case at the West End Hospital the extension projected into the lateral ventricle.

In the third case a diagnosis was made of tumour in the parietal region. Exploration was carried out (osteoplastic resection), and on turning down the dura mater, an extensive hæmangioma was found, with one large venous saccule at the centre. This patient was operated upon two years ago. He had been suffering from fits before the operation, but he had had neither fits nor headache since, so that, as in the first case, operation had done some good.

Dr. F. Parkes Weber said he had listened with extreme interest to what had been said by the three openers. He wished to add a few words in regard to the following question: When cutaneous hæmangiomatous conditions were associated with vascular tumours of the brain, of what type were they? The first chief type of vascular tumour of the brain was the racemose meningeal angioma (probably the cavernous angiomata were allied) above the tentorium cerebelli. It was known that the main kind of angiomatous condition in the skin, allied to this meningeal or cerebral condition, was the ordinary port-wine-stain nævus. What he especially wanted to know, however, was what was the type of angiomatous condition in the skin—in the few cases in which there was any—associated with what might be called and had been called "Lindau's disease"? By the latter term he meant definitely the occurrence of hæmangio-endothelioma in the central nervous system, mostly below the tentorium cerebelli. One would expect that when cutaneous angiomatous conditions were associated with Lindau's disease their histology would be that of hæmangio-endothelioma. He wanted to know whether that was the case. Hæmangio-endothelioma was not a very rare type of cutaneous nævus.

Another remark he wished to make was the following: The meeting had heard about the interesting association of cysts in the kidney (and certain other organs) with Lindau's disease. Of what kind were those cysts in the kidney? It was not the type of renal cyst most generally known. He had taken a special interest in cysts of the kidney and liver; and in what were called congenital cystic (polycystic) kidneys (a familial congenital-developmental disease which was not infrequently familial), one nearly always also found a cystic condition of the liver if there were a post-mortem examination. If cysts in the liver were not seen at once with the naked eye, a microscopical examination would nearly always reveal their presence, or the presence of an analogous interlobular fibrous condition. He had never heard of this condition (which he preferred to call congenital-developmental "cystic dysplasia of the kidneys and the liver") being associated in any way with Lindau's disease. And he would make the challenging statement that whatever kind of cysts there might be in cases of Lindau's disease in the kidney and in other organs, they were not of the class that he called congenital-dəvelopmental cystic dysplasia of the kidneys and liver.

Dr. Henry Cohen said that he had seen a number of these angiomatous malformations of the brain, and they had usually been associated with radiologically demonstrable changes. In the case of a patient, now aged 25, epilepsy (not Jacksonian) had developed when he was a boy aged 15. Recently, after an attack of status epilepticus, a left hemiparesis had developed, affecting, maximally, the left arm. He had the characteristic signs of a right parietal lesion, unassociated with any papillœdema, and he had not had severe headache. There was a bruit over the right parietal eminence, synchronous with cardiac systole and obliterated by pressure on the carotid artery. By X-ray examination one was able to see a little depression in the skull, and, apparently radiating from it, a series of dilated veins of the diploë. The depression seen was due to an angioma arteriale of rather marked type, depressing the inner table of the skull, thinning the bone, and apparently

preventing the return of blood through the diploic veins, so causing this dilatation. There was no direct connection between this depression and the distended veins.

In another case, that of a woman, whose left posterior auricular artery had been tied by Mr. Sewell seven years before on account of pulsating tinnitus, mild epileptiform attacks had developed, four years afterwards, and, later, headache, dysphagia, shooting pains in the left face and jaw, etc. There was a marked bruit, synchronizing with the cardiac systole, over the left mastoid area, and X-ray examination showed that the mastoid and petrous area was thinned out and grooved by this arterial angiomatous malformation.

The next case of interest from a radiological standpoint was one of a female patient who had a port-wine stain over the whole of the left side of the body, and an enormous cavernous type of nævus on the left side of the face and leg. Only in the last three years had any neurological symptoms developed. The patient's age now was 39. Right hemiparesis had developed, i.e., on the side opposite to the port-wine stain, and there was a marked bilateral area of calcification in the skull.

He had just had a case of exostosis of the frontal area, which gave the same radiological picture. He thought, however, that the condition in that case was one of calcification within a nævus.

[Dr. Cohen showed a slide illustrating a case in which a telangiectasis had produced a characteristic Weber's syndrome.

He also showed a slide illustrating a tumour in the right subcortical parietal area. The patient, who had had signs of gross intracranial tension and attacks of hemiplegia, suggesting a vascular origin, had died suddenly. In the tumour were definite lacunæ containing blood, but no definite vessel wall could be seen.]

Dr. W. G. Barnard: I am showing a specimen of a tumour because of its rarity. Dr. Lindau has not seen one of the kind before, and in their monograph Cushing and Bailey doubt the authenticity of the records of those already published, and state that they themselves have not seen such a tumour. It is a capillary hæmangioma of the brain, occurring above the level of the tentorium cerebelli. It is situated in the temporal lobes adjoining the fissure of Sylvius, and the sections show the typical structure of a capillary hæmangioma with fibrous interstitial tissue.

Speaking as a pathologist, I can see no reason for the rarity of these tumours above the level of the tentorium and their comparative frequence below that level, and I suggest that the rarity is probably apparent rather than real, and is due to the fact that the more intensive study of cerebral tumours is of recent date.

[The tumour was demonstrated, the cyst in the substance of the brain, together with the hæmangiomatous tumour in its wall, was shown, and its resemblance to similar tumours occurring in the cerebellum was pointed out.]

Dr. Lindau (in reply) said he agreed with Dr. Greenfield that trauma, and not seldom a serious one, was often an occurrence in the history of these cases, and was a feature which could not be overlooked. On the other hand, he considered that the condition under discussion was congenital, and existed from the beginning as an abnormal collection of cells, later in life giving rise to a neoplasm. Tumours of the acoustic nerve occurred at about the age of 40, probably in the same way, originating from an abnormal collection of cells.

As for capillary angiomatosis, there was an opportunity to observe the development of the angiomata that was quite extraordinary, namely in the fundus. When a case of retinal angioma was followed clinically, now and then the other eye was affected, so providing the possibility of studying the lesion from the beginning. Was it not most probable that the cerebellar angiomata developed in the same manner as the retinal?

He had been much interested in Dr. Russell's figures, and he had been surprised at the number of cases of cavernous capillary telangiectasis she was able to show. He noted that Dr. Russell, also, insisted on the necessity of keeping these growths clear of other forms, such as hæmangioblastomata. She had shown a case in which, besides cavernous angiomata of the brain, there were cysts of the kidneys. He did not think that these formed a link between capillary angiomatosis and angiomatous malformations. In the kidney one could now and then see cysts when tumours occurred in other parts of the body. Much more significant was a cystic pancreas or a retinal angioma; these were not reported in Dr. Russell's cases. He thought it wise to keep the groups distinct.

In answer to Dr. Parkes Weber, who spoke of nævi of the skin correlated with capillary angiomatosis, his (Dr. Lindau's) view was that they were quite rare—contrary to the conditions in cavernous angiomatosis—only two cases being reported (Fabritius, Aust). No histological examination was made in these cases, and we had no knowledge of the type of the associated skin lesions. The cysts found in the kidneys were scattered, only from 10 to 20 in number, and apparently of another kind than congenital polycystic kidneys.

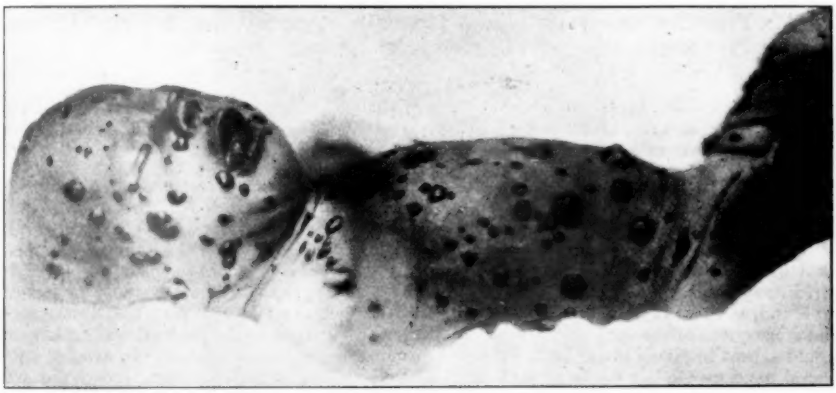
Section of Dermatology.

[*October* 16, 1930.]

Multiple Angiomata.—H. W. BARBER, M.B.

D. B., female, aged 10 weeks. The child is one of twins, the other being normal. There are an enormous number of angiomata of various sizes scattered over the whole body: there are also some on the mucous membrane of the mouth.

Discussion.—The PRESIDENT asked whether, in the experience of Members, cavernous angiomata disappeared spontaneously. He saw a large number in infants and children which were removed with carbon dioxide snow and other methods of treatment, but he had rarely seen them in the adult.



Dr. Barber's case of multiple angiomata.

Dr. A. M. H. GRAY said that in many of these cases the condition disappeared entirely. A small relative of his own had a large vascular nævus, occupying the whole of the back of one hand. The doctor who saw it originally wanted to have it treated, but the speaker advised against it. At two years of age there remained no trace of it. He had seen that kind of thing happen repeatedly. Unless there was some special reason for treating the condition it was his custom to hold his hand for a year or two.

(The publication of this case was deferred in order that the illustration might be included.)

[*November* 20, 1930.]

Extensive Lupus Vulgaris treated with Radium by Surface Radiation.—DUNCAN C. L. FITZWILLIAMS, C.M.G., F.R.C.S.

C. W., male, aged 14. Admitted to St. Mary's Hospital 17.4.30.

Had extensive lupus of the face, which began five years ago in the region of the

nose, and has gradually spread over the face towards the chin (fig. 1: photograph taken 20.4.30).

In addition to the visible lesions, the nose was partly destroyed and both nostrils were completely occluded. The mouth had contracted to a small opening, so that the diet had to be fluid. He breathed through his mouth with a whistling noise. Wassermann reaction negative.

Treatment.—A Columbia paste mask, 15 mm. thick, was made for the face, a hole being left for the mouth to allow breathing.

On this mask were scattered: 10 needles of 1 mgm. of radium, 5 of 1·5 mgm., 6 of 2 mgm., 7 of 0·5 mgm. (equal to 33 mgm. of radium element).

The mask was worn for some hours each day, being removed for feeding, sleeping and washing.

July 20, 1930.—After three months' treatment 16,869 mgm.-hours of radium had been given, and the disease had disappeared from the face except for a small area around the mouth, over which no radium had been applied; even in this area great improvement had taken place. The patient was discharged for two months, but was re-admitted, and has worn a small plaque over his mouth with long radium needles, bridging across the space left for breathing. His present condition is seen in figure 2.

[Mr. FITZWILLIAMS showed ten further cases of rodent ulcer, and one of Paget's disease of the nipple, all treated by radium with satisfactory results.]

Discussion.—Dr. H. C. SEMON said there might be an indication for the use of radium in lupus verrucosus. He had successfully treated one case of recurrent lesions on the knuckles about six months ago and there had been no relapse to date.

Dr. R. T. BRAIN said that a scheme of dosage of radium in the treatment of rodent ulcer was not generally established. Unscreened flat radium applicators had been successfully used for this purpose in dermatological practice for nearly thirty years, and the good results of such treatment were well known. However, more recently, screened radium had been used in the form of platinum radon seeds or radium needles, such as those employed by Mr. Fitzwilliams. The radiations from such a source consisted almost entirely of gamma rays, and, as these rays had much more penetrative power than the beta rays, the absorption—and consequent effect upon the tissues—of gamma rays were so much less. Therefore one would expect to give a much longer exposure when using screened radium. Instead of a few hours' exposure to an unscreened radium plate in close skin apposition, radon seeds or radium needles were applied or inserted for several days. It was accepted that a rodent ulcer was remarkably susceptible to the action of radium, and therefore large doses were not necessary or desirable in treatment. For a rodent ulcer not exceeding 1 cm. in diameter 100 mgm.-hours of screened radium was about the right dose. This dose was often greatly exceeded, and unnecessarily massive dosage was, in his opinion, the principal feature of the cases shown to-day. Some of the cases already showed considerable atrophy of the treated skin, and in one of them there was a little horny papule set in a vascularized atrophic scar.

Large doses of irradiation were naturally indicated when dealing with tumours outside the province of dermatologists, especially when such tumours were squamous-celled carcinomata. A number of small squamous-celled epitheliomata and tar epitheliomata had been successfully treated with radon and radium in Dr. O'Donovan's clinic.

With regard to the treatment of Mr. Fitzwilliams' case of lupus vulgaris, he agreed that the dose of irradiation given was so enormous that severe atrophic changes must inevitably result, and, although the development of squamous-celled epithelioma upon a radium scar was a rare occurrence, yet one felt that the pathology of the treated skin was the same as that following an excessive dose of X-rays.

A few cases of lupus vulgaris had been treated by radon seeds in Dr. O'Donovan's clinic, and it was found essential to cause some necrosis of tissue in order to produce favourable results. This is what one might anticipate, for the peculiar virtue of radium apparently consisted in its action on cells undergoing rapid mitosis, and this was not a characteristic or

FIG 1.—Extensive lupus vulgaris. (Dr. Duncan C. L. Fitzwilliams' case before treatment.)

FIG. 2.—Present condition.

essential feature of a granulomatous inflammation of the skin. Therefore one would not expect radium to have a selective action on lupus vulgaris.

A case of lupus verrucosus had been treated with unscreened radon seeds in order to produce necrosis, and the result was promising. By this technique the destructive process affected all the tissues, both healthy and diseased, as well as the invading organisms, and the same effect could be obtained by diathermy with this difference, that the application of radon was painless at the time, although quite painful later.

Mr. DUNCAN FITZWILLIAMS (in reply) said he would have thought that radium acted in a manner totally different from that mentioned by Dr. Brain. Radium was an antiseptic, and, if it was placed near a bacterium, the organism would not grow. He attributed the satisfactory effect of radium, in cases of lupus, to its action on the bacillus itself, more especially on any form of cell. He thought its action here was quite different from its action in a case of carcinoma.

Two Cases of Alopecia Totalis, showing the Effect of Ultra-Violet Light.—HENRY CORSI, F.R.C.S.

(I) Patient, female, aged 25. Alopecia areata began in 1922; it became worse, and within six months all the hair had fallen from the scalp. Eyebrows and lashes not lost till 1924. Pubic hair was lost, but returned almost at once.

The patient has been in perfect health for over ten years at least. Wassermann reaction negative. The menstrual periods began at the age of 13, and have been normal ever since.

October, 1929.—Mercury vapour light treatment was begun. The hair began to grow in about one month, and improvement has been progressive.

(II) Male, aged 27. All hair fell from the body, within about six months, at the age of 13. Pubic hair grew at age of 17. One year ago the scalp was treated by mercury vapour light. The hair began to grow within two months. The æsthetic effect is now quite good. The occiput is still very thinly covered, but this did not receive much treatment. Eyebrows and eyelashes have grown to some extent, but limbs have remained quite bare. Wassermann reaction negative.

Dr. W. J. O'DONOVAN said that in alopecia areata, mild or severe, he considered general light therapy of the greatest assistance. He had five patients with alopecia totalis of from two to seven years' duration who had done well, but it had required two years' continuous general treatment for the more severe cases. He was not convinced that local applications were more efficacious than rubefacient or blistering treatment.

Plexiform Neuroma.—HENRY CORSI, F.R.C.S.

Patient, male, aged 25. One year ago a tumour began to grow on the forearm, on the line of the ulnar nerve. It feels like a flat disc of tangled string, lying beneath the skin, but superficial to the muscles. It has a diameter of $1\frac{1}{2}$ in.

Erythema Elevatum Diutinum.—ALICE CARLETON, M.B.

The patient, a male, aged 38, developed a nodule on his left arm in October, 1929. When seen in November, he showed a raised vivid erythematous ring of rubber-like consistency, surrounding a flat, slightly pigmented centre. Its dimensions were then 4 by 5 in. The epidermis was movable, though not freely, over the induration, which itself was quite easily movable on the deeper tissues. The ring appeared to widen and break up into scattered nodules. Some of these have now disappeared, but some are still present. In February, June and August of the following year, lesions appeared on the right side of the chest, the back of the neck and the interscapular region. Their appearance and evolution are similar, except

that on the chest the original nodule tends to break up into smaller nodules without any definite ring formation. The lesion on the neck has nearly disappeared.

The first sign of a developing lesion is a rather diffuse hardening, which gradually becomes more salient and circumscribed. Nothing resembling the pearly nodule of granuloma annulare was ever visible.

The patient is a healthy man with no rheumatic history. The Dreyer-Ward Sigma test is negative.

He has received at different times a potassium iodide mixture and X-rays. The X-rays caused temporary improvement, but the lesions have also regressed spontaneously without treatment.

Discussion.—Dr. A. M. H. GRAY said that the case did not correspond to his conception of Darier's centrifugal erythema, which was a much more superficial condition. The edge also travelled faster than it appeared to have done in this patient. The striking general feature in this case was that the lesions were hypodermic, but he could not put a name to it. Weidman, in a paper on erythema elevatum diutinum, written about a year ago, had suggested on histological grounds that this condition was related to that described by Dr. Parkes Weber as panniculitis, to cases of dermato-myositis, to Haverhill's disease, and also to some cases of granuloma annulare. He regarded them all as in some way similar in histological structure to the rheumatic nodule. In one of his cases he had cultured the streptococcus from the tissues. There was probably some relationship between the superficial erythematous plaques, of the type of erythema elevatum diutinum, and some of the equally rare conditions in which there were infiltrations in the fat. The present patient reminded him (Dr. Gray) of one he had seen recently, who had, particularly on the thighs, and to a less extent on the upper limbs, large plaques of infiltration in the fat, with a sharply-marked edge, and a faint salmon-coloured discoloration of the skin—though not with the same sharp ring formation seen in Dr. Carleton's case. He had labelled that case, tentatively, "panniculitis." Unfortunately he was unable to obtain a biopsy.

Dr. W. N. GOLDSMITH said that he had shown a somewhat similar case to the Section.[1] The earliest lesions had been annular, consisting of steep, nearly white rings of rubber-like consistency. Afterwards a very large typical mycosis fungoides tumour developed, arising abruptly from the skin, and having the characteristic histology. But the patient also had a third type of lesion, namely a very deep, plaque-like infiltration, not annular, and hardly raised above the skin level. This last was very similar to some of the lesions in Dr. Carleton's patient, and he wondered whether possibly Dr. Carleton's case might also later be recognized as one of mycosis fungoides.

[P.S. 22.1.31.—After eight injections of a sensitized streptococcal vaccine all the lesions have completely disappeared.—A.C.]

Extensive Hairy Pigmented Nævus.—MARY HORAN, M.B. (for Dr. W. J. O'DONOVAN).

The patient, L. T., a girl, aged 3½, was first brought to the London Hospital at the age of 4 weeks, on account of an extensive pigmented nævus on the back. At that time no abnormal hair-growth was noted on the areas affected.

She was brought to Dr. O'Donovan's clinic on October 23, 1930, with the present gross hairy and pigmentary deformity.

She is a curly-haired, blonde, small, intelligent child. Her face bears so striking a resemblance to the various published illustrations of the Russian Kostroma [1] family, and to others reproduced by Drs. Double and Houssey [2], that Dr. O'Donovan on this ground alone made a provisional diagnosis of extensive hairy nævus before the child was uncovered for inspection.

The mother, questioned about "maternal impressions," gave a history of many dreams of rats, dogs, and other hairy animals, during her pregnancy, but did not attach great importance to this.

1 *Proceedings*, 1930, xxiii, 356 (Sect. Derm. 12).

The parents and the brother, aged 2 years, are healthy, and have normal skins.

On examination the child was found to have a large, pigmented nævus, covered with long dark hair, and extending from the scalp margin behind around the neck to the sternomastoid muscles on either side and covering the shoulders and back over a cape-like area reaching to the tenth dorsal spine. Similar hairy and deeply pigmented moles up to one inch in diameter are scattered on the abdomen, thighs, legs and arms.

REFERENCES.

[1] ZIEMSSEN (H. von), "Handbuch der Speziellen Pathologie und Therapie," *Lancet*, 1873, ii, 616.
[2] DOUBLE et HOUSSEY, "Les Velus," Paris, 1912.

Extensive hairy pigmented nævus.

Discussion.—Dr. W. J. O'DONOVAN said the patient's mother insisted that something should be done, but that the treatment should be both effective and entirely safe. A leading article had appeared in the *Lancet*, 1930, ii, 1082, pointing out the dangers attaching to X-ray therapy of the skin, and he (Dr. O'Donovan) would like to have the opinion of his colleagues as to the propriety of instituting X-ray treatment in this grave case.

Dr. J. D. ROLLESTON said that during the last sixteen years he had seen two cases of giant nævi with this distribution, a condition to which the late Dr. Leonard Guthrie gave the name "tippet nævus." This was a rarer form of giant nævus than the "bathing drawers" variety. When he had shown these cases at the Children's Section,[1] the general

[1] *Proceedings*, 1914, viii (Sect. Dis. in Child., 11); 1926, xix (Sect. Dis. in Child, 7).

opinion was that the conditions were better left untouched, though one Member suggested sending the case to the Radium Institute for advice.

Maternal impressions had been advanced in explanation of these extensive nævi. Bircher[1] had suggested that for a giant nævus to occur there must be a twin ovum, that the violent shock produced by the maternal impression caused a reflex contraction of the uterine muscles which broke up one ovum, and that the partially obliterated ovum was grafted on to the twin brother.

Dr. AGNES SAVILL said she wondered whether it would not be safer to use surgical diathermy in preference to radium or X-rays in such a case.

Nævus Unius Lateralis involving the Sebaceous Glands and Pilo-sebaceous Follicles.—H. W. BARBER, M.B.

J. M., male, aged 18.

This patient has a curious nævus unius lateralis involving the sebaceous glands. It extends from the mid-lateral line on the right side, about 1½in. above the iliac crest, obliquely across the abdomen to the right scroto-inguinal fold, and thence downwards along the inner side of the thigh to the level of the popliteal space.

The nævus clearly involves the pilo-sebaceous follicles, which are dilated and plugged with comedones. At the right scroto-inguinal fold is a cyst-like formation, which has been secondarily infected.

Angioma Serpiginosum.—H. W. BARBER, M.B.

M. W., a female child, aged 4, is said to have had urticaria papulosa since the age of ten months.

The angiomatous lesions appeared two years ago, and have since spread. They consist of oval and circinate rings, resembling in configuration the circinate form of erythema multiforme. They are not raised, and the appearances are very similar to those of Schamberg's progressive pigmentary dermatosis, i.e. cayenne-pepper-like vascular points in a telangiectatic network. From the larger oval lesions smaller circular ones arise—the so-called "infective satellites." The eruption involves the lower part of the chest, the abdomen, flanks, and groins.

Lichen Nitidus.—KNOWSLEY SIBLEY, M.D.

F. H., a healthy woman, aged 27, a typist, has never had a serious illness, or other skin disease, but had a nervous breakdown following measles three years ago, and gives a recent history of some mental worry.

About August, 1929, some minute spots appeared on the front of her right wrist, and these, she thought, more or less disappeared. In April, 1930, they reappeared, and gradually spread up the right forearm, then appeared on the front of the left elbow, the back of the neck, and on the anterior and posterior axillary folds.

Some small scattered papules are also present on the soft palate, and on the sides of the tongue there are some whitish patches, also some irregular white streaks on the buccal mucosa, but none on the genitalia.

The rash on the skin consists of numerous, closely-packed, minute papules, which remain discrete, and do not tend to coalesce. Some are of the colour of the surrounding skin or slightly darker, and many show slight umbilication. There is no itching.

Skiagrams of lungs, mediastinal glands, and of small bones of hands are negative. Von Pirquet and Wassermann reactions negative.

Histological report (Dr. I. Muende).—The general histological structure of the papules corresponds with that of an early stage of lichen nitidus.

[1] *Arch. f. Derm. u. Syph.*, 1897, xli, 195.

Discussion.—Dr. BARBER said that his conclusion about lichen nitidus was that it was merely a variant of lichen planus, as Dr. Dowling and he had seen two cases in which lichen nitidus, typical both clinically and histologically, had been succeeded by equally typical lichen planus. He had shown one illustrative case on two occasions, first, with lichen nitidus, and later with lichen planus lesions. He did not believe in the tuberculous origin of lichen nitidus. He thought this case of Dr. Sibley's corresponded rather to those which had been described as "miliary lichen planus." There was a papule on the wrist which he thought was one of ordinary lichen planus. He had had one remarkable case of lichen nitidus in which the lesion on the buccal mucous membrane was not like that of lichen planus.

Dr. G. B. DOWLING said that the section shown was absolutely typical of lichen nitidus. One point was the erosion of the epidermis from below upwards by the infiltration, causing it to be, in parts, very thin. A second point was the close-set and localized nature of the infiltration; a third was the tendency of the epidermis to enclose the little collection of cells. These points, with the lichen planus lesions in the mouth and the typical lichen planus lesions on the wrists, seemed to settle the problem as to the identity of lichen nitidus with lichen planus.

Dr. A. M. H. GRAY said he wondered if Dr. Barber and Dr. Dowling had considered whether there were two distinct diseases—one lichen nitidus, and the other lichen planus miliaris. This had been suggested by some observers.

Lupus Erythematosus in a girl, aged 8.—A. M. H. GRAY, C.B.E., M.D.

This case was brought because of the age of the patient. The child has on each cheek red, discoid patches, which have a raised scaly edge, and a flat, smooth centre, in which can be seen a number of dilated follicles with horny plugs. The condition is of six months' duration. The lesions are typical of lupus erythematosus.

The child gives a positive tuberculin reaction, and a skiagram of her chest shows some doubtful enlargement of the paratracheal glands. Otherwise nothing abnormal was found.

Dr. O'DONOVAN said he had under treatment at present a child, aged 5, affected with the disease, and he had previously shown one, aged 8, in whose case the condition had begun a year previously.

Angioma Serpiginosum.—A. M. H. GRAY, C.B.E., M.D.

The patient is a married woman, aged 27. She believes she was bitten by an insect on the right thigh and right leg in April, 1930. Red spots appeared at these sites, and fresh ones have come out in the neighbourhood. She has now a collection of reddish areas, varying in size from that of a lentil to that of a two-shilling piece, on the outer aspect of the upper third of the thigh and on the outer side of the knee. The lesions are rather ill-defined, reddish patches, and in them can be seen a number of bright red vascular points, which do not disappear on pressure. Looking at the surface of the skin by reflected light there is a suggestion of atrophy of the skin. Outside these patches a number of isolated, small, red spots, like cayenne pepper, can be seen.

A portion of one of the lesions was removed, and sections show marked swelling of the papillary and sub-papillary layers. There is much swelling at the most affected part, and the epidermis over it is stretched. At the edges of the patch, round the capillary vessels, commencing round-cell infiltration, with some swelling of the endothelium of the vessels, can be seen. In the more affected part the endothelium is markedly thickened, but the vessels appear to be patent. The perivascular infiltration appears to be very marked, and consists chiefly of lympho-

[1] Vol. xiv, No. 8, p. 73, June, 1921.

cytes, but here and there plasma cells are visible. There is some secondary involvement of the epidermis by stretching and œdema of the deeper layers. The appearance presented is similar to that described by Wise and Pollitzer in their classical article on angioma serpiginosum (*Journal of Cutaneous Diseases*, 1913, p. 725).

Dr. Adamson suggested that this case might be one of Schamberg's disease, a question which is generally raised when such cases as these are demonstrated. I think, if the patient is examined in a good light, it can be seen that the red spots are vascular and not pigmentary and that there is a marked erythematous zone surrounding them, which, in my experience, is absent in Schamberg's disease.

Paronychia due to a Yeast-like Organism with Curious Discoloration of the Nails.—G. W. BAMBER, M.D. (for Dr. A. M. H. GRAY).

Patient, female, aged 36, a housewife.

History.—The condition began one year ago with inflammation at sides of nail of left thumb. There was no discharge from beneath the nail-fold about this time. Three months ago a similar condition developed round the nail of the left index finger. Since the onset an occasional bead of pus has been squeezed from the nail folds.

Present condition.—Nails of thumb and index finger of left hand are of mahogany colour on all parts not covered by nail-fold: below this nails normal in colour. Colour easily removable by scraping. Nail-folds of left thumb swollen all round and tender, that of left index finger swollen on radial side, also tender. No pus from beneath either fold. Thumb-nails show irregular transverse grooving. Index-finger nail shows slight separation from the bed on radial side near free end.

Bacteriological examination.—A yeast-like organism from both nail-folds. No clotting of milk. No liquefaction of gelatin.

Reactions:—

Glucose	...	...	acid and gas	Saccharose	...	faint acidity
Maltose	...	...	acid and gas	Salicin		

Peptone water: A fine mycelium bearing conidia.

Discussion.—Dr. J. E. M. WIGLEY asked whether any investigation had been carried out to ascertain the presence or absence of monilia in apparently normal nails.

Dr. H. MACCORMAC said that he too was inclined to think that in many cases a monilia was merely saprophytic. On one occasion he had obtained a pink monilia from warts beneath the nail-fold, and this had increased his suspicion as to their pathogenicity in other cases in which their causal relationship might seem more definite.

Dr. DOWLING said he thought monilia, even perhaps *M. albicans*, were normally saprophytes, but that they could take on pathogenic characters under suitable conditions. In Dr. MacCormac's case, warts—by damaging the nail-fold—might have provided these conditions. The usual cause of paronychia was cooking or wet household work of any kind. In America a number of cases were recorded by Kingery and Thienes, among those engaged in the fruit-canning industry. Cultures of monilia grown from these cases were inoculated into the nail-fold of the investigators and an acute inflammation of the fold was produced, demonstrating that at that moment the fungi had become pathogenic.

Dr. A. M. H. GRAY said that it was obvious that the inflammation must be caused by something. Pyococci had not been grown, and it was therefore at least probable that the yeast-like organism was responsible. He was mainly interested, however, in the pigmentation; the patient said she had not put anything on the nail before the pigmentation appeared. Monsol was not applied until the nails were their present colour, and iodine had not been used. Since she had used perchloride of mercury and spirit, the new nail was growing its normal colour.

Acne Agminata (Acnitis of Barthélemy).—W. N. GOLDSMITH, M.D.

H. S., male, aged 25. Cinema operator. Ten weeks ago noticed something "under the skin." Within three weeks the eruption had developed to its present state in which it has since remained largely unchanged. When I saw the patient on October 14, 1930, the lesions were rather more vivid red and pustular, and the onset had been so rapid that I thought the condition might be a pustular folliculitis induced by the carbon fumes and oil to which he is exposed in his work. No history of bromide or iodide having been taken. Wassermann reaction negative. During the last five weeks the lesions have remained practically stationary. They consist of brick-red conical papules, mostly with a pustular centre, confined to the face and especially marked in the naso-labial folds. Tuberculin reaction (von Pirquet) positive.

Biopsy.—A section is shown under the microscope. A biopsy was performed on November 11, 1930, by Dr. I. Muende, who reported the histological structure as that of papulo-necrotic tuberculide. The infiltration is not very sharply circumscribed, is intense, and is composed predominantly of small lymphocytes with a fair number of large giant-cells. There is no resemblance to Boeck's sarcoid, except in some of the deeper nodules.

The patient also has a pre-existing acne vulgaris, but he is very definite in his statement that this eruption developed to its full extent within three weeks, and that he has never had anything similar before. The positive tuberculin reaction has no great significance, especially in this case, since 25% of acne vulgaris cases are positive even to one in a million of old tuberculin. (Martenstein and Noll.)

The eruption is unusually profuse and symmetrical.

I do not know whether this condition is the same as that described by Tilbury Fox as follicular lupus. Probably there is a series of intermediate types of follicular tuberculosis of the face, ranging from the relatively acute papulo-pustular, or papulo-necrotic, to the more torpid sarcoid variety, depending on the phase of immunity of the skin. Though in this case the condition developed rather abruptly and pustules seemed to be forming from the beginning, the deeper portions of the infiltration have the histological structure of a sarcoid, whilst the more superficial portion is like an inflammatory lupus vulgaris. Cultures are now being made from several pustules with the object of enabling us to decide whether, as Dr. Gray suggests, the suppuration is only secondary.

Acne Agminata.—G. B. DOWLING, M.D.

This patient, male, aged 34, came to me eight months ago, having had acne agminata three months. There were not anything like the number of lesions that Dr. Goldsmith's case presents, and these were smaller, but characteristic with the typical occurrence on the eyelids. The patient, has been treated with solganal, having been given 3 grm. altogether. Small doses only have been administered, the largest being 0·25 grm. The lesions have almost entirely disappeared. There is now a little superficial scarring, in place of these lesions. No other treatment has been applied.

Lupus Vulgaris in Vaccination Scar.—R. T. BRAIN, M.D.

A girl, E. C., aged 12, attended Dr. O'Donovan's Clinic recently with a history of vaccination in May, 1929. She had had two pustules on the left arm ; the upper one healed normally, whilst the lower lesion remained inflamed, and the central part only eventually became pale. Her mother and a sister were vaccinated at the same time, and they had normal reactions and healing.

The patient has slightly enlarged cervical glands. She has no cough or other

signs of tuberculosis. On the left arm is an upper sound, supple vaccination scar 1 in. by ¾ in. in size. Two inches below this is a second scar of which the upper and lower crescents show the apple jelly infiltration characteristic of lupus vulgaris, and the surface is slightly crusted.

Clinically there is no doubt of the diagnosis, and the case is shown because of the extreme rarity of lupus appearing as a local sequela of vaccination. It is true that the condition is mentioned in the larger textbooks, and no doubt it was much more common when lymph was used from individuals or from animals infected with tuberculosis. In the present case the lymph came from an approved reliable source, and, on inquiry, there was no recorded instance of any tuberculous or other lesion appearing on a vaccination scar obtained with this particular lymph.

The patient's father has a seven years' history of phthisis. He has been certified, and sanatorium treatment was advised but refused. The possibility of the father having sucked off the lymph from one lesion was considered as a mode of infection, but inquiry elicited the fact that both parents were in favour of vaccination, and had no wish to interfere with its natural course.

There remains a possibility of external infection of the open sore, but it would appear to be unlikely that the entering bacilli could develop so rapidly as to prevent initial healing of the vaccinial pustule. It is suggested that, following dissemination, tubercle bacilli found a favourable site for development in the vaccinial lesion.

Dr. J. D. ROLLESTON said he would like, after thirty years of fever practice, to emphasize the extraordinary rarity of any cutaneous sequelæ of vaccination. The only three cases he could recall in this period were (1) a case of post-vaccinial psoriasis, which he saw at a meeting of this Section nine years ago[1]; (2) a case of keloid in vaccination scar; and (3) a morbiliform eruption following primary vaccination in a young man who had been sent to hospital as a case of measles.

Lupus Erythematosus treated with Sanocrysin and Bismuth.—HENRY MACCORMAC, C.B.E., M.D.

The patient, D. P., aged 26, first noticed the lesions on the backs of her fingers in autumn, 1929; they were then considered to be "septic chilblains." They persisted throughout the summer, and additional lesions developed in a V-shaped area on the exposed skin of the chest, and on the cheeks and nose. The patient's previous history is satisfactory, apart from an enlargement of the glands in the neck.

In June, 1930, she was taken into hospital, and had four injections of sanocrysin, amounting to 1·2 grammes in all. Definite improvement followed, but the eruption subsequently relapsed, extending over the nose and cheeks in a mask-like distribution. In October, 1930, a series of bismuth injections was commenced. This brought about an immediate and marked improvement; there are still distinct traces of the eruption on the face, but the condition on the chest has completely cleared up, and is much improved on the hands.

I have seen similar results in other cases under my care, treated with bismuth in which sanocrysin has either failed entirely, or has caused only temporary, improvement. In this case the eruption may be included in the tuberculide group by reason of the presence of well-marked tuberculous glands in the neck. Thus a form of the disease, presumably tuberculous, has proved responsive to bismuth, although bismuth has not been considered to have the specific application in tuberculosis which is possessed by the gold-salts.

Discussion.—Dr. A. C. ROXBURGH said he had treated a number of cases of lupus erythematosus with bismuth and gold, and after unsuccessful treatment with gold he had seen some clear up under bismuth, in the way Dr. MacCormac had described. Dr. Feldt, when

[1] *Proceedings*, 1921, xiv (Sect. Derm., 12).

he was in this country, advised using both gold and bismuth on the same day, thus enabling smaller doses of each to be used.

The bismuth preparation which he (the speaker) had used had always been a suspension of the metal, so that the improvement could not be due to quinine in his cases. In the cases recorded by Dr. Corsi and himself at the Joint Discussion with the Section of Medicine early in 1930,[1] it appeared that the results of gold injections were the same, whether the patients were tuberculous or not.

The PRESIDENT and Dr. J. L. FRANKLIN referred to a case which improved under initial treatment with krysolgan, and was later given a few injections of sanocrysin. The latter caused an acute exacerbation of the eruption on the arms. Six injections of bismuth were then given, and the eruption subsided considerably. Another course of krysolgan was instituted, and the patient recovered completely.

Dr. WIGLEY said he had had two cases which had failed to respond either to gold preparations or to bismuthyl.

Dr. DOWLING said that the efficacy of gold compounds in the treatment of tuberculosis had only an indirect connection with the tubercle bacillus, but apparently it was very closely concerned with the type of lesion which the tubercle bacillus created, namely, a very chronic lesion tending to become enclosed in fibrous tissue. Lupus erythematosus was also a chronic inflammatory lesion, and that alone might explain the efficacy of the gold compounds in its treatment. Dr. Lyle Cummings had demonstrated by histological investigation in tuberculized rabbits that sanocrysin, by setting up an inflammatory reaction around a tuberculous lesion, allowed the normal defensive action of the body fluids to be brought into play. The gold itself did not appear to destroy tubercle bacilli directly.

1 *Proceedings*, 1930, xxxiii,

Section of Obstetrics and Gynæcology.

[*November* 21, 1930.]

DISCUSSION ON THE INTERIM REPORT OF THE DEPARTMENTAL COMMITTEE ON MATERNAL MORTALITY AND MORBIDITY.

Dr. T. Watts Eden: The Committee was established with very wide powers of reference, but one of the most important subjects was the inquiry which they undertook into a series of maternal deaths. I think the result of this inquiry has several very interesting features. With the exception of the section dealing with the training of medical students, the rest of the report has no novel points. The inquiry was conducted by local Medical Officers of Health. Every doctor or midwife who had the misfortune to have a maternal death received a schedule, and these were filled up and sent back, and the information was supplemented by personal interviews where necessary. Of the 2,000 cases, in over 400 the death was due to associated disease, in a number of others to extra-uterine gestation, and others had to be rejected because the information was not sufficient. So the number comes down, eventually, to 1,286.

The Committee set themselves to try and track the cause of death in each case, by attempting to discover what had gone wrong with the management of the case, and they have evolved what I think is a very useful formula, viz., "the primary avoidable factor." That is to say, in considering the circumstances of the case, they endeavoured to pick out the point at which, in their judgment, the management of the case had first gone wrong, and they called that the "primary avoidable factor."

In less than half the cases did they succeed in discovering anything that could be called the "primary avoidable factor"; in 660 of the 1,286 cases the inquiry drew a complete blank as regards the explanation of the maternal death, except, of course, the statement of the cause of death, such as sepsis, or hæmorrhage. In 626 cases a "primary avoidable factor" was discovered and the factors have been grouped. It is interesting to notice that in 35% or 36% of the cases in which a "primary avoidable factor" was found, that factor was, in the judgment of the Committee, some error on the part of the doctor or of the midwife. We must not assume that the "primary avoidable factor" is the same thing as the cause of death; very often it is only an indirect cause of the fatal termination. Again, if they found two faults, e.g. failure of ante-natal examination and, afterwards, a too-early application of forceps, followed by sepsis, that was classed as failure of ante-natal care, though the more immediate cause may have been the injury which the patient received during delivery.

One or two things which come out of the inquiry are very interesting. The number of deaths which occurred during normal labour is surprisingly heavy, because 40% of these 1,286 cases showed what would be called obstetrically a normal labour. And the occurrence of sepsis in normal labour was very high indeed. There were 319 cases of normal labour in which the patient died of sepsis. Of those 319, in 232—that is to say, in about three-fourths of them—they could not discover even a "primary avoidable factor." In these two crucial subjects, the cause of death in normal labour and the frequency with which sepsis follows normal labour, the report does not help us at all, and these points are the kernel of the whole question of maternal mortality. We know how to deal more or less successfully with things like accidents of labour, but we do not know why we get so much sepsis in normal labour, and why, in what is technically normal labour, there should be such a high mortality. In these things, we could hardly expect that

the inquiry would help us very much. At the time the inquiry was set up, a number of obstetric teachers, concluding that not very much could be expected from it, wrote to the *Times* as follows:—

"Inquiries into maternal deaths by the officers of the local health administration would be useful in showing where there is a lack of hospital accommodation, provision for the removal of urgent cases, and such like, but would add nothing to our knowledge of causes, and without that knowledge prevention is impossible."

I suggest that the Interim Report shows that that estimate of ours was not very far wrong.

The Committee have spent a good deal of time in estimating the frequency of abortion, but as there are no statistics it is almost as difficult as the Hebrews found it to make bricks without straw. The practical point about miscarriage is, I think, the lack of institutional facilities for treatment. Cases of miscarriage are "obstetrical outcasts"; no hospital wants them, and if the Committee could have made some suggestion as to how to get more accommodation, it would have been useful.

As to the recommendations of the Committee about training of students, there are one or two things of a general character that I would like to say.

We have been asking for years for increased facilities for training our students, and I hope we shall give these recommendations the best consideration we possibly can. It looks as if the Ministry of Health were saying to us: "You have been wanting something of this sort for a long time; here is what we are prepared to try to help you get." And I think we should not turn it down unless, in our judgment, it is quite impracticable. And supposing that, for the moment, what is asked is out of reach, it seems to me we have a very useful opportunity before us now, in that we shall be in a position to say to Government: "We would like to do all this, but we have not enough cases to do it with. If you will provide us with the means of getting extra cases, to the number we want, we will see that it is done." At the present moment the Government and the Local Authorities together would probably be able to place at the disposal of obstetrical teachers greatly increased facilities for training their students, and for post-graduate training also, as part of the use of the new hospitals which have recently come under the Municipal Authorities. We may never get another opportunity like this, and it seems to me we ought to make of it the most that we possibly can.

Dr. J. S. Fairbairn: To my mind the startling feature of this Report is that there has been agreement without reservation among thirteen pundits, and all of them professing medicine in one shape or another. So strange a phenomenon is it that it gives me furiously to think and wonder whether there is anything in this Report which really matters to allow of this almost unnatural unanimity. I have been through it, and have found that what is already accepted has been said again very nicely, and its chief merit is its summary of the present position regarding maternal mortality.

I agree with Dr. Eden that the data on which the causation of avoidable factors in maternal deaths is based are too vague and unscientific to permit of reliable conclusions, and I do not feel that the Committee has advanced our position in this regard. Its Chairman, however, thinks otherwise, for he says in his Annual Report for 1929 (p. 21) of the Reports of the two committees appointed by his Department, that a study of them "will make clear the large body of common agreement which has now been reached in regard to the facts of the position. Whilst it is true that the Reports contain comparatively little which is entirely original, they have brought together for the first time, and correlated, the various aspects and factors of the problem. We now know more or less exactly where the shoe pinches."

In my opinion the Chairman is too optimistic, and my contention will be that the various aspects and factors of the problem have *not* been brought together and

correlated, because the greatest and most important factor of all—the lying-in woman who provides the mortality in question—does not receive adequate consideration in the Report. I am not at all sure that the Report has not placed the shoe-pinch on the wrong foot altogether. The patients themselves and what they demand from their attendants have been crowded out by these same attendants with their accompaniments in the shape of hospitals, clinics, and other material resources, and are scarcely in the picture.

It will hardly be questioned that the last fifty years have witnessed a slowly developing but rapidly accelerating change in the attitude of mind of the whole community towards childbearing and all it involves—and in other countries as well as our own. Neither the women of to-day nor their menfolk are prepared to take the bearing and rearing of families as a matter to be left in the hands of Providence, as was the custom of their grandparents and great-grandparents. Births are restricted and spaced, and when failure to do so occurs they do not think a demand for the removal of the unwelcome guest is unreasonable, though any qualms on the doctor's part may be so regarded. With these spaced and less frequent pregnancies there is also a more insistent call for adventitious aids to an easy delivery and more and more the services of the medical attendant have been diverted from their true purpose of securing natural function and the removal of the causes of its disorder to relieving pain and shortening the duration of labour.

No better instance can be given than the recent agitation for wholesale anæsthesia, a question fully discussed in the Report in the light of advice given to the Committee by various bodies. We all accept relief of the pangs of labour as one of our duties, but with the proviso that it must not interfere with our primary object of securing normal function and that we must be left to decide when and how it should be given. But they who pay the piper call the tune, and the women and their belongings expect relief as soon as the pains become troublesome and call for "the baby to be taken away" as soon as they have had enough of its coming. Possibly a time may come when substitutes for the natural powers may be adopted in all cases of childbirth without adding to maternal mortality, morbidity, and subsequent disability, but that time is not yet, and my argument is that all our right hand has gained by better obstetric knowledge and technique is now being squandered by our left hand using this skill on occasions tenfold and more than is justifiable for strictly medical reasons. These are often termed euphemistically, but wrongly, as "humanitarian," and are defended, particularly in America, on the ground that parturition is a pathological rather than a physiological process, hence necessitating medical attendance. Surely this social aspect, represented by an alteration in the spirit and attitude of mind in which maternity is approached, is one that should be taken into early consideration by a Committee called to advise on the application of present knowledge to the problems of maternal mortality? It is a change in social habits which must be accepted, for it has come about, and with which we have to reckon; also it has very important bearings on the structure of a national maternity service such as is envisaged in the Report.

Its practical consequences are seen in interference (1) with conception, (2) with pregnancy and (3) with labour. The first must result in a relative increase in the proportion of primiparous labours and in this way in a raising of the risks of childbirth. The second means an increased resort to provoked abortion. This is fully discussed in the Report, and the conclusion is reached that evidence has not been forthcoming to support the opinion that "an increase of deaths from abortion, of sufficient magnitude materially to affect the maternal death rate, has taken place in recent years." The effects of increased interference in labour are considered only so far as they may be due to anæsthesia and analgesia, in the chapter devoted to that subject. The views of the various medical bodies consulted are there given on anæsthetics in labour, but nothing is said of the widespread demand of the public for an early delivery.

So important do I consider the social factor in maternal mortality that, if the Committee wish suggestions for future research, I will mention an inquiry into the variations in the maternal death-rate in different social categories. There are many surmises offered to explain the reason for the lower rate in the slum areas than in the better housed areas of our large towns, and in yesterday's *Times* I happened to notice the report of a discussion on the subject in which the Medical Officer of Health of one of our large cities said

"Statistics showed, without being able to give the reasons, that the rate in the wealthiest district of Leeds was the highest in the city, whereas it was lowest in the poorest quarter where the people did not get the good food obtained by the residents in the wealthy area."

The Aberdeen Report showed the same thing and in the one under discussion the results selected as the best are from poor districts (p. 106). Its comment on these figures is given in italics and runs "What is being done for some women can and should be done for all." I would have rewritten it and in leaded type thus, "*What some women do for themselves can and should be done by all normal women.*" I have recently seen some very striking figures collected by a chief Inspector of Midwives in a rural English county which seem to show that the nature of the attendance on labour is not of itself the all-important factor that would be gathered from this Report. They were collected for the 12 years, 1907-18, in the hope of showing the improvement of the trained over the untrained midwife, but were not made use of because they failed to show what was expected.

Attendant	No. of Births	No. of Deaths	Rate per 1,000
Untrained midwife	7,278	14	1·9
Trained ,, ...	*21,900*	*50*	2·2
Total by midwives	29,178	*64*	2·1
Other than midwives	*43,823*	*177*	4·02
Total live births in the county	73,001	241	3·3

I might add that the still-birth rate in these various categories corresponds precisely with the maternal death-rate. Question may be raised as to the reliability of these figures and as to what is to be argued from them, even if accepted. All I can say regarding them is that they were collected by a very capable and conscientious Inspector of Midwives with full knowledge of the midwives working under her, with access to office records and in the expectation that they would show the opposite of what they do. I offer them only to indicate that the class of attendant may not have the importance that would naturally be assigned to it and that possibly the type of patient dealt with has a much greater weight than has hitherto been laid on it. Those mothers satisfied with a *bonâ fide* type of midwife would be lower in the social scale than those who would try to have a Queen's nurse-midwife and certainly than those who would engage a doctor. On this basis the mortality-rate rises with the social status of the women attended.

The Committee must have been fully aware of this social factor. I cannot imagine that what I have myself written on the subject was unknown to them.[1] Jellett has something to say on it in his book on "Maternal Mortality," and in the Annual Report of the Scottish Board of Health for 1928 Dr. T. F. Dewar includes among the hindrances in the endeavour to lower maternal mortality,

"undue or premature or indiscriminating interference with the natural process of parturition,"

and goes on to say

"The desire of the accoucheur . . . to alleviate and cut short the patient's present suffering is natural and praiseworthy" . . . "the patient herself or her relatives may be clamouring for his active assistance and may regard his unwillingness to yield to their entreaties not as the evidence of the self-control and the wise restraining judgment that it really is, but as the indication of lack of skill or experience on the one hand or of an understanding sympathy on the other." . . . "It is helpful towards a true and fair grasp of the situation if it is agreed that the medical attendant in such cases has often to make a difficult decision under trying, even distracting, circumstances."

1 "Obstetrics," Chap. V. Oxford Medical Handbooks, 1926.

In his Report for 1929, from which I have already quoted, the Chairman of this Committee shows clearly that he has fully recognized the importance of this social change, for he there says (p. 29),

"social habit and aspiration in regard to large families are undergoing profound changes. In some sections of the population there is, from one cause or another, a growing disinclination for children, and a progressive disposition to find medical relief for the disabilities of childbirth."

It is unfortunate that this aspect of the problem has not been considered in the Report, for one really useful function that such Committees can perform is, when necessary, to be the mouth-piece of unwelcome truths that must be told to the public; as it is, poor individuals like myself get the odium that should fall on their broad backs. I have learnt from bitter experience that there is no more unpopular task than to tell an audience of women that a price in maternal mortality must be paid for relief of pain and the artificial shortening of their time in labour. It is received so icily that it gives one the shivers and is regarded merely as a dodge of the medical profession to shelter themselves and throw the blame on others.

Clearly, this social change must be taken into account in laying down the principles on which a national maternity service is to be based, for it is gradually pervading all ranks of the community, though it has not yet influenced greatly the class that is satisfied with a midwife attendant. Hence any scheme should be designed to perpetuate and encourage this hardy midwife-employing class, and care taken that the foundations are laid on a service of midwives for normal labour in a way that will tend to eliminate the idea that medical aid is required for such labours. Although the Report says that exact comparison of the mortality-rates of different countries cannot be made (p. 8 and 9) the conclusion it draws may be accepted—that the Scandinavian countries and Holland have much lower rates than ours and the U.S.A. a much higher. I cannot forbear from quoting its final paragraph on this matter; it reads

"The low death-rate in the Scandinavian countries and in Holland has been frequently noted and not fully explained, although the great attention paid to the training and status of midwives in these countries probably plays an important part."

Nor can I forbear from digressing to draw attention to the habit this Committee has acquired of thinking in terms of the attendants in labour rather than of the women in labour. Differing from them as I do in this matter, I will re-write for them the last sentence thus:—

. . . although the custom of the women in these countries of choosing a midwife as their attendant probably plays an important part, for it shows their confidence in their power to fulfil the reproductive function without artificial aid.

It is these countries where the women employ midwives that have the low mortality-rates, while if you go to the U.S.A., where they have no midwives and probably more machinery and other meretricious aids to parturition than anywhere else in the world, there is the peak of the maternal mortality. Do not let us "go west" to the U.S.A., but east or north-east to Scandinavia, if we want to lower our maternal death-rate.

Such evidence as we have of the comparative rates in our own country tends to show the same thing, and there is no need for me to do more than refer you to the page (106) from which I have already quoted, for figures from the various hospital and district practices that are taken to illustrate that what is being done for some women should be done for all. But I would point out to you that included in them are the figures of the Queen's Institute, where the women are attended by midwives not of the selected order that obtains in hospital districts and the doctors called in to their aid are the local practitioners, and yet the results are on a par with the others. Credit must be given to the parturient women; they are a selected class, but *self*-selected, and, like the Scandinavians, they expect to see the thing through themselves and have the hardihood to do so.

The midwives, through the Council of their Institute, have expressed themselves as dissatisfied with the ill-defined nature of their position in this Report, and I must say that on reading the sections of the Maternity Scheme proposed, it almost looks as if the midwife would become a mere maternity nurse, and that I feel would be wrong. The end of Section II, on p. 109, seems to indicate something of this kind. Difficulties will doubtless arise if the family practitioner does not have full experience of normal labour and comes to regard his function as that of being called in to finish it off artificially. Yet a block-fee to cover all maternity services, midwife, doctor, etc., opens the way to other difficulties. Remembering how the sickness claims of women under the National Health Insurance Act exceeded the actuarial calculations, we cannot but fear that when the women know that they have a call on a doctor they will have him out and do their best to have their money's worth, whether he is required or not. I trust that some means will be found to obviate this danger.

My criticism of this Report has almost entirely been on a sin of omission, which I have termed the social factor, and regard as of greater moment than any sins of commission which there may be in the Report. Some, however, may think that I have overstated my case, and, in concluding, I would like to make my position clear by shortly summarizing what I want to be taken as my case.

Because I have laid so much emphasis on the social factor, both possible variations of custom and habit in different social strata, and change in outlook on the whole reproductive function, I do not wish to exaggerate its influence. I have only made an effort to redress what I consider a lack of balance in this Report. Information on this matter is insufficient to allow of dogmatic assertion, but, with our present knowledge, I plead for a recognition of the possibility that social conditions and habits may influence maternal mortality so far as to counteract some of the results of improved attendance and resources. Hence the perspective of the Report cannot be correct without taking much more account of the social factor. Its section on "Some Social Aspects of the Problem" (pp. 34 to 39) is wholly insufficient and too much occupied with the useless relation of odd cases of disasters.

My references to the demand for the relief of pain in labour are not to be taken as evidence that I am opposed to efforts in this direction. I have said that this demand must be accepted as an accomplished fact in all women who employ a doctor, and as such must be reckoned with.[2] I have fought so hard for the extended use of sedatives in labour, and particularly for the teaching of their use to midwives, that I have obtained an unenviable reputation as the arch-druggist among obstetricians. I would go further than the Report does, and than most of my colleagues, in allowing a modified use of sedatives and anæsthetics by midwives. The securing of normal labour is now largely become a problem of how the effects of emotion and fatigue from continued pain can best be avoided without interfering with the physiology of parturition, and I regard it as the big problem of modern midwife practice. The relief of pain from childhood onwards has made the whole population less capable of its endurance, and my point is rather that this natural consequence must be given greater consideration, especially the study of the individual patient and what best will meet her needs. Unfortunately, I can go no further, but I have a feeling that our results will not improve till more than lip-service is given to "Obstetrics as a Branch of Preventive Medicine," and that term is translated into our practice. Unfortunately this Report does not help my ideals to the degree I had hoped for.

Dr. W. H. F. Oxley: As I am a member of the Committee, which is still sitting, I did not intend to intervene in the discussion, but as it is quite clear that neither of the two speakers has read the report or even understood the terms of

[2] "Sedatives in Labour," *Brit. Med. Journ.*, 1929, i, 753.

reference, perhaps I may be allowed to read these, with the object of keeping the discussion on useful lines. The Committee was appointed to "advise upon the application to maternal mortality and morbidity of the medical knowledge at present available," and the second part was "to inquire into the needs and direction of further research work."

That is to say that this Committee was asked, as consisting of practical men, to advise the Government, not the profession, as to what practical steps can be taken to make available to every woman in the land, the best medical knowledge we have now, and so to reduce maternal mortality. Dr. Eden's criticism that nothing fresh has been found out as to the cause of sepsis following normal labour, is therefore beside the point, and would probably not have been made had he read the reference more carefully. Some of Dr. Fairbairn's criticisms were really praise, and might almost have been quotations from the pages of the Report itself. I hope he will read the Report carefully after the meeting, and find out what really were the recommendations of the Committee.

Professor R. J. Johnstone: I should like to put one point. I am very sorry I had not the opportunity of speaking before Dr. Fairbairn. I think the most important part of the Report is the recommendations with regard to the training of medical students. I shall not offer criticisms on those recommendations; they are to be considered at a meeting of the General Medical Council next week, of which I am a representative. I think we have here a representative collection of obstetric teachers, and I would like to hear from them what they think of these recommendations. I have read only one criticism of them, by Professor Munro Kerr, who puts two pertinent questions. The first is, "Is it possible for the teaching schools to put these recommendations into effect?" The second question is, "If they are put into effect, will they be successful in giving us a type of obstetric practitioner who will be safe for the lying-in woman?" He answers both in the negative.

As far as the second question goes, I think he goes too far. He seems to have in mind the type of obstetric practitioner who would be an obstetric consultant, who would be competent to perform any obstetrical operation and deal with obstetric emergencies. I do not think the General Medical Council aims at producing that type of general practitioner. There is a phrase employed in actions for malpraxis, in the question whether the defendant has used *reasonable skill and judgment* in his treatment of the case. What the General Medical Council is concerned with is to ensure that every man, before he is let loose on the public, will at any rate have the knowledge which will enable him to use "reasonable skill and judgment." We cannot ensure that a man uses reasonable judgment, but we can ensure that students shall have reasonable knowledge and skill; and I ask whether obstetric teachers here think that those recommendations will ensure that the student gets reasonable knowledge and skill.

Lady Barrett: The openers have brought forward two important points. Dr. Eden pointed out that no cause was found in half at least of the number of maternal deaths investigated; that is a very important thing to have brought to our notice, even if the Committee had done no other work, because in deaths from sepsis, for example, it drives us to look for some other source than contact sepsis only. We must realize that there are other forms to be investigated, and observations made in regard to hospital work support this.

Dr. Fairbairn said that one important factor which the Committee neglected was the woman herself. I quite agree that the woman herself is the factor which should be considered first. But I was disappointed when Dr. Fairbairn went on to explain that the woman, in his opinion, apparently brings about a large amount of the ill results because of her unwillingness to bear labour long enough, in consequence

of which forceps are applied, or at least some interference is made, in many cases in which it is unnecessary, and when the woman would be better off if she were left to nature. I was hoping that Dr. Fairbairn was going to remind us that exhaustion in the mother renders both sepsis and hæmorrhage more liable to occur—both important causes of maternal mortality—and if the woman becomes more exhausted by going through a long labour without help, i.e., without relief of pain, then relief of pain which also abolishes undue interference with normal labour must be seriously considered as a factor in maternal morbidity.

Dr. Fairbairn has pointed out the extraordinary lack of ill-effects in very unfavourable surroundings, and that is difficult to explain. Many have suggested the possibility that these women, living under such bad conditions, have become immune from infection, but there is also an unfavourable aspect of the social conditions of the mother which renders it difficult for her to carry out either the instructions to attend antenatal clinics, or to do what she is advised at these clinics. The Report gives several cases in which women were advised to attend and did not do so, and cases of women who were given definite instructions what to do—to go into hospital, etc., and did not obey. The social conditions of the child-bearing woman in the home form part of the problem. No woman can look after children in the home and yet go into hospital and be ill. The difficulty of these women is a very real one, and until it is faced and provision made for some free time in the day and some facility for home work in time of illness, I do not think you will get the whole population of England, as desired by the Committee, to come under the Rules, which were devised according to the medical knowledge which at present exists.

Mr. W. Gilliatt: I shall deal only with Professor Johnstone's question. The suggestion in the Report that each student should deliver thirty cases instead of twenty cannot be carried out at present, as there are not the number of patients available in institutions where students are taught. Should this suggestion be adopted, I fail to see that there will be any improvement in medical education unless the General Medical Council and (or) the examining boards insist on the regulations being carried out, which they do not at present. Mr. Comyns Berkeley's figures of the number of cases delivered by students in different parts of England bear out the fact that they do not now deliver twenty cases.

Professor Dame Louise McIlroy: The value of the Report is the crystallization of the opinions expressed by those who gave evidence before the Committee. It embodies much that has been advocated by obstetricians for the last ten years.

The value of the 2,000 cases investigated is questionable, as the Committee themselves found that the data supplied were inaccurate. The general impression, after reading the recent speeches of the Minister of Health, is that almost half the deaths could be avoided. This looks as if the doctors and midwives were to blame. On reading the Report, however, another impression is given, that is, that the primary avoidable factor is not always preventable under the present condition of affairs. In the classification of maternal deaths a much larger number might be attributed to sepsis. For example, deaths from pneumonia are frequently due to sepsis, but are usually regarded by the medical attendant as a separate complication rather than an extension of puerperal sepsis. Embolism is frequently septic in origin. Much depends upon the patient herself and her power of resistance and recuperation. The *vis medicatrix naturae* of the pre-Lister days was a preventive factor even though antisepsis was unknown. In antenatal work the multipara should have most attention. The primigravida requires most in labour, and institutional treatment is therefore more necessary for her. The Report very properly stresses the value of trained obstetricians for antenatal work. The doctor in charge of a clinic should have the responsibility of the patient through her

confinement, or should be called in by the midwife when required. All obstetricians will welcome facilities for the better training of medical students. If training centres would fulfil the conditions laid down by the General Medical Council as to the personal conduction of twenty obstetrical cases, an advance would be made. It is impossible for most teaching hospitals, under present conditions, to obtain thirty cases for each student.

Mr. Donald Roy: In answer to Professor Johnstone's question, I think that if these Interim Report suggestions could be carried out in their entirety there would be a vast improvement in the quality of doctors turned out as a result of the improved obstetric teaching, but it is of no use for speakers to turn round and upbraid Examining Bodies or the General Medical Council for not insisting on requirements which it is impossible to carry out at present. In common with other people here, I have tried for six or nine months to get some agreement among the medical schools so as to approach the London County Council for its co-operation by permitting the use of its maternity cases for teaching purposes. But it is hard to get solid agreement among the medical schools or solid support. This is the only practicable measure which is immediately possible. It needs to be brought home to the authorities at the medical schools, so that we can get a push from behind to bring it about.

Then Dr. Eden referred to the meeting of obstetric teachers ten or twelve years ago, when in common with other optimistic people I thought something would be done. The suggestion was to have two or three, or more, central teaching obstetric hospitals in London which would provide sufficient experience for the students. The position with regard to obstetric cases has become worse since then, but we have now at any rate the opportunity for making a very definite advance towards getting the cases, but not an opportunity for carrying out the ideal suggestions brought up ten years ago. When the medical schools as well as the teachers of obstetrics are agreed, then something will be done.

I find myself in agreement with very much of what Dr. Fairbairn has said, partly because I had my obstetric training in the same maternity hospital, where physiological obstetrics was and is still carried out to a much larger extent than in the country as a whole.

The question of anæsthetics is a very difficult one, because if you have the courage—as Dr. Fairbairn has—to say that a return to physiological labour is really what is wanted to prevent a good deal of unnecessary interference, you are liable to be accused of being a very callous person who is disregardful of the pain which women suffer. You must look beyond the pain and take a long view of the welfare of the woman. It is remarkable to me how different the point of view about parturition and what it entails appears to be between the majority of the delicately-nurtured classes and the hard-working women with whom one is familiar, and also whom one enormously admires, who has her baby, for example, south of the river or in an agricultural district. The point of view from which these different people approach parturition seems to be very important. These poorer women know, probably from intimate contact often from an early age with labour cases and from their friends, exactly what normal labour is. They know that it is in ordinary cases a natural process and not a very dangerous business. They approach the question of having their babies with knowledge of what it means and with confidence in their safety. Their morale is good from the beginning, they have complete confidence in the trusted maternity institutions and their whole attitude is different from that of some of their richer sisters. In the latter, knowledge of parturition either does not exist or is largely obtained from the gossip of their friends which is made up of the awful fatalities they have known and experiences they have suffered or think they have suffered, and these have been passed on from one to another, so that they approach the question in an attitude of fear.

With them there is great ignorance of what is really going to happen and the fear that goes with it leads to a desire for anæsthetics or assistance at all costs. There is definite need for education, not so much of the women who are attended in maternity hospitals, as of their richer—but not really more fortunate—sisters, in this matter of maternity. And that would go some way to bring together the totally different points of view of these ladies who are pushing anæsthetics first and all the time and the ordinary view of the more conservative obstetrician who wishes to relieve the pain and exhaustion of labour so far as is wise, but also to keep labour cases which are normal as physiological as possible.

Here are two experiences of the value of such education; one I know of from personal knowledge, the other was told to me by one of the visiting staff of a maternity hospital. Having read this correspondence in the lay Press about the terrible, devastating pains of labour, a certain municipal body went to the Medical Officer of Health of the district and said "We must at once have anæsthetics for all our labour cases." This Medical Officer of Health, who was very broad-minded and wise, said: "I do not know anything about it; we will go to the nearest lying-in hospital." There they went as a deputation and were met by my friend and he conducted them round the wards where many smiling women were seen who had been delivered, some a few hours, and others immediately before the visit. And he said "Ask these people any question, ask about their experiences." This deputation, which came like Balaam prepared to curse, went away with an entirely different idea of what were the after-results of a normal physiological labour unassisted in these cases by any anæsthetics.

Precisely the same thing happened at another maternity hospital at which I work. Two women of the richer class told me their experience and that they felt some sense of shame at their inability to tackle their labours in the same spirit as the women in the wards, who they could scarcely believe had been delivered only a short time before their visit, as they were quite free from signs of a painful experience and from shock.

There can be no serious departure from the view that exhaustion and shock should be combated by morphia, anæsthetics or timely assistance as indicated, but there is a marked difference of opinion as to the frequency of the occurrence of exhaustion and shock following the normal labour of normal healthy individuals.

If there is evidence of undue exhaustion appearing, it should, like any other departure from the normal, be treated on ordinary obstetric principles, weighing any disadvantage the treatment may carry.

It is not fully brought out in the Report that the institutions held up as examples as giving "excellent results and the lowest mortality," are just those in which the bulk of the patients, attended by midwives under skilled supervision, are treated on conservative physiological lines and anæsthetics employed only for obstetrical indications. It would be expected by some, therefore, that these hospitals would show a high incidence of exhaustion and shock, with its consequences reflected in a high maternal mortality. The evidence, if these results have any value as evidence, is either that exhaustion and shock are adequately combated by conservative methods of practice and anæsthesia for purely obstetric indications, or that it does not occur in these institutions to any great extent, and in any case that it is not a factor of importance in these institutions in causing maternal mortality. This conclusion must afford the management of these hospitals some satisfaction and encouragement to proceed on the same lines, though the Report gives no indication of any intention to imitate their sound practice.

Dr. G. W. Theobald said he considered that the student was inadequately educated and that the general average practitioner had not the time to carry out conservative midwifery.

He criticized the opinions which had been given as to the nature and size of

maternity hospitals. He did not consider that students could be so well trained in the maternity department of a hospital having 16 beds as in one in which there were 200 beds, and he believed that if it was necessary for students to live in a maternity hospital it was equally necessary for the instructor to live there or close by. Therefore the system must be altered.

After studying a map of England, leaving out Wales and Scotland, he considered that if forty hospitals were built they could be so placed that the great majority of women would live within five miles of such an institution, and no woman would have to travel more than twenty miles. It was better for a woman to travel twenty miles in a modern ambulance and receive expert treatment than to travel two miles and be treated by other than a specialist. It was obvious that we needed maternity hospitals where a student could live, where there were many cases, and to which any woman in the country could be sent in an ambulance.

Professor F. J. Browne said he felt very much in the same position as Dr. Oxley, that as a member of the Committee, he was not called upon to defend the Report. He thought it must have been forgotten that this was only an *interim* report, and so what Professor McIlroy had said with regard to research work on shock was a little premature. While he did not feel called upon to defend the Report, he would have to correct misstatements of fact, and these, in this case, were so many that he found it difficult to believe that either of the openers of the debate had read the Report carefully.

Dr. Eden had said that the Report made no reference whatever to deaths occurring in normal labour. He (the speaker) was sure that was one of the chief things in the minds of members of the Committee during the time they were sitting—the mystery of these deaths in normal labour. He was very doubtful if sepsis ever followed properly-conducted normal labour. Before we advanced any further with the solution of this problem of puerperal sepsis, it must be realized that it was necessary to apply to normal labour the principles of Listerism.

He asked the openers to turn to page 18, on which that question was dealt with *in extenso* :—

" A large proportion of deaths followed normal labour, and in the majority of these cases there was no positive evidence of any mismanagement during delivery."

The Report did not say there was no mismanagement :—

" It must not be assumed, however, that the methods were satisfactory."

The reports were so scanty that where facts were missing it had to be assumed that the facts were not known. Practitioners put in a few drops of lysol and thought they had made an antiseptic solution. In other words, the Committee had in their minds all the time that if normal labours were properly conducted, deaths would not occur. If the principles of Listerism were properly applied, there would be no puerperal sepsis. He was a firm believer in that.

Again, dealing with the question of abortion, Dr. Eden had said there was great need for institutional treatment of abortion, and that the Committee had made no recommendation regarding that ; if he turned to page 45 he would find that they had in fact made such recommendation. They found that the provision for the treatment of these cases was inadequate and recommended hospital accommodation.

Dr. Fairbairn had dealt with one particular phase of the report, and said that no attention had been given to the woman herself, or to the fact that her psychology had changed ; she was less tolerant of pain and demanded early interference. But the whole Maternity Service scheme which the Report recommended was based on a recognition of that fact ! It had been advised, for example, that normal midwifery should be taken out of the hands of the doctor, because it was known

that if a doctor were present he would, perhaps, yield to the importunity of the patient and interfere before he should do so.

Mr. Gilliatt had said that the General Medical Council would not enforce even their own Resolutions, but if the Council and the Licensing Bodies accepted the recommendations of the Committee, the teaching authorities must fall into line. For the first time explicit recommendations had been framed that admitted of only one interpretation; most important of all, a form of final certificate had been recommended that demanded more definite information than had ever been asked for before, and it had been laid down that the certificate must be signed by the person directly responsible for the student's teaching in midwifery and gynæcology.

It was difficult to see how anything better could have been formulated, The educational recommendations had been criticized in some quarters on the ground that it was impossible to educate the undergraduate up to the required standard. A critic of the Report in the *Spectator* had recommended that midwifery should therefore be in the hands of a specialist service. A woman usually preferred, however, to have her own doctor, and there was no means of preventing it. The only solution therefore was that which the Committee had proposed, namely, raising the standard of training of practitioners as a whole.

In reply to Professor Johnstone he thought we could get the cases. The students at University College Hospital obtained at least twenty-five cases, and by correlating the work with that of State hospitals, it would be possible to get thirty and more.

Mr. Comyns Berkeley: We have with us this evening a member of the Educational Committee of the General Medical Council, and he has asked the teachers present to let him know what they think of the scheme for educating the medical student in midwifery and diseases of women in the Interim Maternity Report.

I can assure Professor Johnstone that everything recommended in that Report, with reference to the training of students, can be carried out at the hospitals, except, for the moment, the number of cases.

With Mr. Stevens and Mr. Roy I am sitting on a sub-committee of the Voluntary Hospitals Committee, which is considering the question as to whether the L.C.C would be willing to provide the extra cases required. The L.C.C. can do this, and, I feel sure, would do it if the authorities of the hospitals expressed a wish to this effect. The great majority of the hospitals in London cannot provide sufficient cases for their students. I trust that the General Medical Council will insist on the course of training laid down in the Departmental Report. No student should be signed up for his final examination unless he produces written proof, countersigned by the obstetric surgeon, that he has attended the stipulated number of cases.

Dr. Fairbairn (in reply): If, as Dr. Oxley says, the Committee, in view of its terms of reference, has nothing to do with the cause of maternal mortality, why did it spend so much of its Report on the results of its investigation into maternal deaths? A discussion of this kind is useless unless it is critical, and surely it is justifiable to point out that a committee called on to advise on the application of medical knowledge to maternal mortality should have given more consideration to one of the recognized factors—the social one—in that mortality?

Professor Browne complains that I have not sufficiently studied the Report, and he may be right, but I have read it carefully enough to grasp its main purport, and, though it may be possible to pick out paragraphs and sentences here and there, I am prepared to stand by my argument that its perspective is wrong in one respect.

I think the Committee has obtained some very useful hints from myself and the others who have spoken, which, if acted upon, should lead to a material addition to its next interim dividend when declared.

Section of Psychiatry.

[*December* 9, 1930.]

Stigmata of Degeneration in Relation to Mental Deficiency.

By Noel H. M. Burke, M.R.C.S., L.R.C.P., D.P.M., D.M.R. & E.

Introduction.—The general subject of degenerative stigmata has been dealt with at so great a length, over so many years, and by so many writers, that it would seem a rash adventure to attempt a further study. The literature includes such names as Féré and Bourneville, each responsible for many papers from 1870 to 1890, Talbot, 1880 to 1907, Bland Sutton from 1890, and Sir Arthur Keith. The subject was considered, with an enormous literary reference, in many pages of the "Traité de Psychologie Pathologique," by A. Marie, in 1910, while smaller studies of individual cases or special anomalies are numbered by the score.

Is it, then, worth while to tread the ground again? Even so hackneyed a subject should be reviewed from time to time, in order to find if any fresh evidence has come to light, or if the old evidence may have acquired a new meaning by reason of advances in other branches of knowledge. It may be possible, also, to fill such gaps as may have been left in the presentation of the subject. It may even be possible to support or disprove the accuracy of earlier statements and theories.

In the present instance I submit a study of 3,000 cases of mental deficiency; I attempt to bring together various aspects of the subject which have usually to be studied separately, I test the validity of the supposed relation between mental deficiency and physical stigmata, and I discuss the possibility that a study of these matters may help to throw light on the causation of deficiency.

The Nature of the Material.

Since it was opened for the reception of defective patients in 1912, there have been received into the Fountain Mental Hospital in Tooting nearly 4,000 patients, of whom the majority have been children of the lower grades. The policy governing the use of the hospital has varied from time to time, so that a proportion of adults of both sexes were housed at one period. To make a homogeneous series I have included in this study only male and female patients up to the end of the sixteenth year of age. There is no very special reason for choosing this particular age as the upper limit except that it has for some years been the nominal upper age-limit for the female patients, who have then been transferred elsewhere. There is, however, good reason to confine the investigation to children, because the very high death-rate amongst young defectives, a death-rate that is peculiarly selective of certain types, causes groups of higher age to be unrepresentative of the problem of deficiency as a whole. In an investigation of recent epidemics of infectious disease it appeared that the mongols and the microcephalics were thus selectively destroyed. This matter is still under consideration, and certain possible errors have to be estimated and allowed for, but the broad fact of this selective death-rate is unlikely to be contradicted. If, therefore, one desires to study such a question as the comparative occurrence of developmental anomalies in each type of defective, one must study a series in which each type is fairly represented.

The material has been divided into three groups: (A) Cases admitted from 1912 to 1916. (B) Cases admitted from 1917 to 1930. (C) Cases still in hospital, these having been excluded from group B.

The records of group A were compiled by a number of medical officers, who worked under rather difficult conditions, and in the early days of the knowledge of deficiency. Both internal factors and those external to the hospital would tend to influence the nature of the notes. In 1917, also, a new system of case-recording

was instituted. Group B was studied almost entirely by one man, an enthusiast for such observation, interested in the physical aspect of deficiency, and working during a time when deficiency was becoming well understood. It is likely, therefore, to show a higher proportion of physical anomalies than group A. Group C, those still in hospital, was specially examined by me with the definite object of finding stigmata. Though a small group, it represents the subject of a completely uniform investigation.

In reading through the 3,000 old case records, it has been interesting to observe the evidences of the varying interest of the several writers. For two or three years there are careful notes of routine Wassermann and similar examinations; at another time physical measurements, at another, neurological examinations, were the main interests. Something of this fluctuation of emphasis is found even in the records of the second group, though the work of a single man. Indeed, this is inevitable. We all become especially interested at various times in a particular part of our work. By contrasting these three periods thus selected, one should get a measure of the importance of the observer as a factor when assessing a value to the numerical findings, and the whole series should be large enough to justify, at any rate tentatively, certain deductions.

Definition.—Marie says that stigmata of degeneration are "characters that do not belong to the race. They appear in an individual, or are susceptible of transmission, but in that case they show up the family as being apart from the race." It is difficult, but necessary, to distinguish such characters from the results of intra-uterine, or of infantile, diseases or accidents.

Morselli [1] gives the following classification:—

A. Pathological effects: (1) Anomalies of development—asymmetry. (2) Effects of constitutional disease—rickets or congenital syphilis. (3) Trauma.

B. (1) True degenerative characteristics leading to deviation from normal type by exaggeration or modification of parental characters. (2) Anomalies leading to deviation from normal type and to a degree of inferiority by arrest of development—hare lip, cryptorchism. (3) Reversive anomalies, i.e., atavistic—prognathism, long simian arms, etc.

I should prefer to include such anomalies of development as asymmetry in the degenerative, rather than in the pathological, group, except in such cases as can be shown clearly to be results of disease or injury. The conditions I include under the title of stigmata of degeneration are those in which there is disturbance in rate or direction or harmony of development, conditions revealing disorder, aberrance, exaggeration, or incompleteness of growth. I prefer to call them developmental anomalies, two words which are completely explanatory and include all the forms, and which avoid the use of the suggestion of degenerateness. I am not quite sure how far degenerateness is a true quality of these conditions, a point to which I shall refer again.

Marie, in his article, does not always follow his own definition of stigmata, but includes conditions that are definitely the results of disease. I may err in the opposite direction by over-caution, but I propose to exclude all asymmetries and deformities in which there is even a remote possibility of causation by neurological or other disease. The essence of the idea of a developmental anomaly is much the same as that which distinguishes primary amentia from secondary amentia and from alienation. Development must have gone wrong rather than have been made to go wrong.

Discussion of Cases Seen.

Working within this definition I now come to a description and discussion of the cases of developmental anomaly that have occurred among mental defectives, confining myself in the main to such cases as I have seen myself.

General aspect and physique.—There is no doubt that mental defectives are poor specimens of the genus *Homo*. The facial features are often unpleasing, the

height and weight are below the normal. Marie, quoting figures from groups of French individuals of various types, shows that the lowest readings and the lowest average readings in measurements of height and weight were furnished by the defective types. Indeed it is permissible to suggest that the defective is an example of development whose anomaly is generalized rather than localized. There are, however, a fair number of exceptions, of good stature, with pleasant features, and in any case I have, as yet, no personal collection of figures to offer, and the point is not important.

Spina bifida.—There is not a single example of this condition, in any shape or form, among the 600 cases in Group C. Five, of which I have seen one, are reported in the previous groups, all apparently slight cases, judging by external appearances.

Considering the large number of helpless and paralysed children amongst those under review, it seems strange that more cases of spina bifida are not to be found. I am told that they are absent even from Leavesden, where cripples are congregated. The chief explanation of this must be that they do not live. Of 647 deaths attributed to spina bifida in one year in England and Wales, 615 occurred in the first year of life [2], and these figures give a measure of the chances of survival of any severe case. But where are the milder cases? Can it be that this anomaly, though essentially involving the nervous system, has a low correlation with mental deficiency? Certainly, the one boy whom I saw in another hospital showed comparatively little mental defect, though very considerable helplessness of body.

There are two systems to consider in the embryology of this type of spina bifida. In the development of the spinal bony system the neural arches of the vertebræ grow out, and, in the cartilaginous condition, complete the arch round the neural canal in the fourth month of intra-uterine life, ossification beginning to replace the cartilage of the vertebræ in the third month. Failure of this arch formation is a part of the story of spina bifida, and means that something has gone wrong with development before this period; how long before it is hard to say.

The other system concerned is the nervous system. In the third week the medullary folds are beginning to close along the centre of the canal and thus to form the neural tube. The neuropore should close at the end of the fourth week, the caudopore just after. Failure of closure of the caudopore produces a cystic spina bifida. Failure of closure of the anterior end of the canal leads to anencephaly. Anencephaly, of course, does not come directly into the picture of mental deficiency, and, according to the present investigation, cystic spina bifida in any degree is also to be excluded. The question to be considered is whether all these conditions are matters of degree of action of some common factor, which may influence the development of the embryo at different ages and to different extents.

Meningocele.—One such case occurs in group *B* and was for a short time under my care. She is a medium grade imbecile and has been able to go home to the care of her people.

In this region in the fifth month the occipital fontanelle projects upwards between the sides of the widely separated cartilaginous tectal plates. These should unite in the middle line soon after birth, and failure produces cerebral meningocele at its common site. (Fig. 1, p. 14.) At what date does development become arrested in this condition? Is it as late as the latter half of fœtal life, or is it determined by some condition at an earlier stage?

This child had also the head deformity known as scaphocephaly, which Keith [3] ascribes to early arrest of growth, or synostosis, along the sagittal suture, with compensatory growth to the shape shown in the photograph. He suggests the possibility of an endocrine explanation.

Cleft palate and hare-lip.—The face is built up, as Keith puts it, round the functions of smell, mastication and respiration, with a central scaffold of smell structures.

At the end of the fourth week five processes appear from the base of the cerebral capsule—four lateral, one central. All are well marked by the end of the sixth week and united by the eighth.

Failures among the several unions that are necessary lead to hare-lip, cleft palate, and macrostoma. Union is performed by the spreading of mesoderm across the line where the two epithelial layers are in contact, as in the healing of wounds, and this union proceeds perfectly in so many cases that it is a question why it should ever fail. When it does fail, is the failure due to conditions in the eighth week or was it ordained at some earlier date?

FIG. 1.—Meningocele.

In the present investigation there were found in groups *A* and *B* eleven cleft palates and two hare-lips, in group *C* three cleft palates and one hare-lip.

Deformities of ears.—Asymmetry, a difference in size or in pattern between the right and the left, is found in a fairly large number of the cases in each group, redundant auricular processes in three. From the sides of the first gill cleft are developed six opercula or tubercles whose growth, fusion and modification make the pinna of the fully formed individual. The pinna begins to take shape by the third month. There is room for much variation in the mammalian ear, depending partly on its functional necessity. It is absent in the whale, while in the seal it is rudimentary and in appearance not unlike the sessile cervical auricles seen in man [2]. These latter are fairly common in many animals, particularly the goat, and were frequently pictured in the goat's semi-human mythical friends, the satyrs and fauns.

In the series of mental defectives under review there were found thirty-nine asymmetrical and six deformed ears, and three accessory auricles, as already mentioned.

Eyes.—Another instance of the failure of closure in an embryological gap is that of coloboma.

In the fourth week the optic vesicle grows out from the side of the fore-brain and forms the optic stalk and the optic cup, which later form the optic nerve and the eyeball and retina. Into the cup is invaginated the lens, during the sixth week. It enters by the choroidal fissure on the under surface of the cup, and has connected with it the hyaloid artery. The choroidal fissure closes, in the same way as the lip and palate and other clefts, and should be obliterated by the eighth week. Persistence of the cleft leaves a coloboma of the iris or of the choroid.

FIG. 2.—Supernumerary auricle.

I can recall only one example in a defective, a boy in another hospital; there is record of coloboma in only two of the whole series under investigation. There are, however, a fairly large number of other instances of anomalous development of the eyes, such as microphalmos, congenital cataract, congenital dislocation of the lens. For one reason or another, in the whole series of cases, sixty-six patients were congenitally blind or seriously impaired in vision. Further, I learn from Dr. Tyrrell that he sees among defectives a considerable number who have errors of refraction which are so extreme in degree or unusual in mixture that they can only be explained as cases of anomalous development.

Hypertelorism.—There is, in my series, no case of interorbital hypertelorism so extreme as those described by Muir in the *Edinburgh Medical Journal* [4], but

there is a fair sprinkling of cases in which eyes are set unusually far apart. The explanation which Muir gives is that there is an anomalous development of the wings of the sphenoid which causes spreading of this part of the face.

There is also in my opinion, though Muir does not mention the possibility, a less common condition that might be called hypotelorism. Asymmetrical or unilateral hypertelorism is another variant which was first described by Sheldon and Lightwood [5]. Of this I found a number of examples in a series of 200 patients measured in another hospital, in the course of an investigation which is not yet completed.

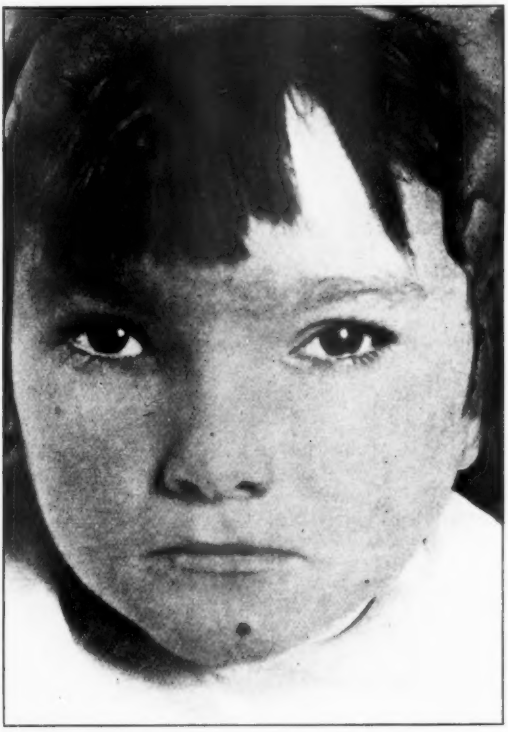


FIG. 3.—Hypertelorism.

Teeth and jaws.—It would require a dentist to give a satisfactory account of dental anomalies in mental defectives, and I shall say very little on the subject. Dentition is notoriously delayed and the teeth are often irregular in shape or arrangement, with supernumerary or absent teeth in a number of cases. I have seen two examples of teeth arranged in a double row like a shark's. One was in a post-encephalitic imbecile in another hospital, another was in a feeble-minded ex-soldier of the war period. Two such were recorded in groups *A* and *B* of my present series.

The jaws which, as a result of civilization, have in modern man become narrow and leave too little room for the teeth, and overlap to produce the scissors bite, may in the defective, give an exaggeration of this form, or may repeat the earlier form

FIG. 4 (*a*).—Asymmetrical face with hypertelorism; direct photograph.

FIG. 4 (*b*).

FIG. 4 (*c*).

FIG. 4 (*b*).—Composite photograph of two right halves of face shown in fig. 4 (*a*).
FIG. 4 (*c*).—Composite photograph of two left halves of face shown in fig. 4 (*a*).

with a wide free arch and massive strength. Another defect, to which my attention has been called by Mr. Pomeroy, is the "open bite" in which the two jaws are so shaped that when the molars meet for chewing there is still a space between the incisors which thus can never meet to bite through the food.

Associated with the shape of the jaw is the shape of the palate, notoriously high and narrow in the defective, but quite frequently broad and well formed. I have not attemped to collect figures of palatal types as yet.

Supernumerary nipples.—The attempt at mammary development on the part of sweat glands, at points along the mammary line other than those customary for the particular animal, is not very uncommon. Nevertheless there are only six examples in the series, all of a very rudimentary type, showing a suggestion of nipple and areola and sometimes only the areola with no recognizable nipple.

Hermaphroditism.—It is true that in each individual there are the elements of the sexual structures of both male and female types, but the development of these elements seems to pursue a unitary sexual course in the great majority of cases. The problem of "The Well of Loneliness" depends on psychological or on endocrine factors rather than on more overt conditions of the immediately sexual apparatus. Indeed, the human partial hermaphrodite, like the "free martin," is probably completely sterile, and unlikely to suffer from sexual interests of a very strongly charged kind. The sexual gland of the free martin shows the incompletely developed condition of an undescended testicle [6]; in a case described as "hermaphroditismus verus" in man, the imperfect gland was undescended and of mixed ovarian and testicular structure [7]. I can give no microscopical evidence on these points from my series, but there are two slight examples of partial hermaphroditism, a male in group *A* and a female in group *C*. The former had a hypospadias which was described as "very closely simulating the female vagina"; the latter has a distinctly scrotal development of the labia majora and a penile development of the clitoris.

Anomalies of hands and feet.—Of all the possibilities of congenital maldevelopment of the extremities, those found in the cases under review consist only of syndactyly, polydactyly, and brachydactyly. Webbed, or partly webbed, fingers or toes are one of the more frequent of the anomalies found. It is only recently that a beginning has been made in routine X-ray examination of such conditions in my hospital, so it is not possible to describe the bony condition of previous cases. There are only two cases of webbed fingers and five of webbed toes in the present hospital population described under group *C*.

Polydactyly has a few representatives, of which one is very interesting. This little girl came in with a history of a sixth finger and toe which had been removed in infancy. There was left the hand with a diminutive ring finger which on radiographic examination showed absence of the proximal end of the metacarpal bone. The other hand looked broad and was found to have a union of the same ends of the third and fourth metacarpal bones, with various aberrant conditions in the wrist structures. As a contrast to this case another shows a long fourth finger. Indeed the series shows increase or decrease of length or size of most fingers or toes in turn. The short and incurved little finger is very common, but group *C* shows one boy with incurved index finger of rather strange appearance. The more gross anomalies that have been described in the literature are absent from the series.

Analysis of the Figures.

In group *A* there were 951 cases, the male being to the female as 5 to 4.
In group *B* there were 1,525 cases, the males slightly in excess of half the total.

TABLE I.—STIGMATA RELATED TO DEGREE OF MENTAL DEFECT.

	No. of cases	Stigmata	Percentage
Idiots	1,067	85	7·0
Imbeciles	1,397	118	8·4
Feeble-minded	12	0	0·0
All cases	2,476	203	8·2

FIG. 5.—Syndactyly in a mongol.

FIG. 6 (*a*).

FIG. 6 (*b*).

Right and left hands of an epileptic idiot.

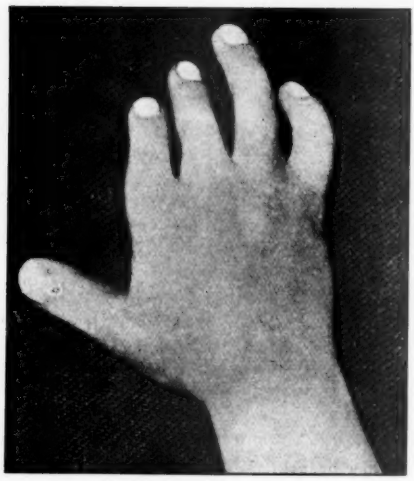


FIG. 7.—Short index and third fingers.

FIG. 8.—Long index finger.

FIG. 9.—Double thumb.

Table I (p. 18) gives an analysis of the two sets of figures combined, and shows the incidence of physical anomalies in relation to degree of defect. The striking thing that appears is that there is no difference in the proportion of anomalies in proportion to the degree of mental defectiveness. The feeble-minded group is obviously too small to have any significance, but the groups of idiots and imbeciles, with over 1,000 in each, should have statistical value.

Various criticisms may be offered, the first obvious one being that the grading may be at fault. It is undoubtedly very difficult, in the borderland of each grade, to determine whether an individual should be placed in one class or another, but I have tried to get a uniform standard by reading through the whole of the notes on each case, and re-assessing the degree of defect for myself. In this process some have been moved up and some down, and I am confident that the idiot group is unchallengeable. The imbecile net is always a wide one, but I am fairly sure that not more than 5% at the most would be put down, by another observer, to the idiot class, while I doubt if as many as 1% would be raised to the dignity of feeble-mindedness. If it be conceded that the grading is substantially accurate, then it must be taken that the figures are strong evidence that there is no relationship between degree of defect of mind and degree of anomaly of body. To clinch the matter there is required a similar set of figures from someone who has access to a similar group of the feeble-minded.

Now this is a result for which I was not prepared. It seems to me that, if there is a relationship between mental deficiency and these anomalies, as everyone declares, it is reasonable to expect to find a closer relationship in patients of a low grade than in those of a high grade. Indeed, it was this idea that set me, two years ago, to explore the question of hypertelorism, when the same puzzling result appeared. My argument was like this: It is said that hypertelorism is commonly related to mental deficiency, and, if that be so, one should find many examples among mental defectives, particularly among the lower grades. Pressure of other duties has delayed the completion of this investigation, and I have not yet measured a series of normal individuals, so that I cannot answer the first question, but it did appear that there was little, if any, relationship with degree of defect.

Goddard, however, in 1912 reported that defective stature occurs proportionately to the degree of mental defect.

TABLE II.—STIGMATA RELATED TO TYPE OF MENTAL DEFECT.

	No. of cases	Stigmata	Percentage
Simple	942	76	8·0
Paralysed	546	46	8·4
Hydrocephalic	70	7	10·0
Epileptic	542	34	6·2
Syphilitic	53	0	0·0
Cretin	33	3	9·0
Microcephalic	90	6	6·6
Mongol	200	31	15·5
All types	2,476	203	8·2 %

Table II gives the incidence of physical anomalies among types of defectives in the same series.

It appears to show that among all defectives the incidence is 8·2%, and among the individual types it is within two units of this central figure in one or other direction, with two exceptions. There is interest in studying both the uniformity of some and the variance of the others.

On general principles one would expect that the paralysed and the hydrocephalic groups would contain a considerable proportion of cases of secondary amentia

which, on present teaching, is not due to racial degeneracy but to environmental conditions. The paralytic group shows a figure almost identical with the average, and it is a group large enough to have statistical value. The hydrocephalics numbered only 70, and I am inclined to deny much value to its high percentage of 10. I do this, more particularly, because in the study of the detailed figures I felt that there was an unrepresentative patch which falsified the general tendency of the readings.

The cretin figures are open to similar criticism as a small sample, though one would expect, on a pricri grounds, a ratio not much below the average. The syphilitic figures, again, are open to discredit, because the total is small, and because it is not fully documented by Wassermann control. In a period of 18 years one finds waves of fashion in medical interest, and syphilis hunting has been in and out of fashion in this period just as has the search for asymmetrical ears or webbed fingers. Still, one would not expect congenital syphilis to be a valid cause of anomalies of development such as the two mentioned, and I think the percentage is not far from a correct one. Finally, the mongols, in 200 cases, have nearly twice as many anomalies as the average for all defectives, and that figure is obtained after excluding those conditions, such as epicanthus and small simple ears, which are part of the condition of mongolism.

Now this result is what I had expected, though I am not sure that it is supported by the general opinion. Brousseau is contradictory, for in one place she says that "anomalies of the extremities are infrequent," and in another that they occur frequently [8]. Tredgold does not give the impression that mongols have more of these anomalies than other defectives, and I am inclined to believe that he does hold this neutral opinion.

Incidence related to sex.—The series under analysis showed 1,312 males with 123 stigmata, and 1,164 females with 77 stigmata, so that the male ratio is 9·3% and the female 6·6%. The difference is possibly large enough to be significant, but I am not at the moment prepared to discuss it.

TABLE III.—STIGMATA IN GROUP C.

		No. of cases	With stigmata	Percentage
Males	Idiots	34	8	23·7
	Imbeciles	190	46	40·2
	Feeble-minded	9	0	0·0
Females	Idiots	49	8	16·3
	Imbeciles	291	52	17·8
	Feeble-minded	10	0	0·0
Total		583	114	19·5

Group C.—I have not discussed Group *C* with Groups *A* and *B*, because it is not absolutely comparable. Just as Group *B* shows a greater proportion of anomalies than are noted in Group *A* so, and for the same reason, Group *C* shows more than twice as many as occur in the figures already analysed. This goes to prove that if one is looking specially for these things one finds them, whereas if one is merely doing a routine examination, one notices just the striking points. Further, to notice and to make a written note are not necessarily one and the same thing. It is all a matter of personal interest. For this reason my own series is again not comparable, because I have included anomalies which others might have considered insignificant.

My figures, on analysis, give the same lessons as do Groups *A* and *B*, but my average percentage of anomalies in 583 cases is 19·5 per cent.

TABLE IV.—STIGMATA RECORDED IN GROUPS A AND B.

		Total
Eye conditions	15 cataract, 14 deformities, etc. (2 coloboma, 2 glaucoma), 30 blind	59
Ear conditions	asymmetry 34, "deformed" 5, accessory auricle 1	40
Face conditions	asymmetry 7, "fœtal" 1, hypertelorism 2, deformed nose 1	11
Head	asymmetry 5	5
Hare-lip	... ...	2
Cleft palate	partial 4, degree not specified 7	11
Teeth	double row 2, absent incisor 1, other irregularities unlisted	3
Accessory nipple	1 right, 1 left	2
Heart conditions	patent foramen ovale 3, congenital heart 21 ...	24
Hermaphroditism	hypospadias 1	1
Congenitally short leg ...	right 1	1
Precocity (? pituitary) ...	2	2
Nævus	2 (nævoid amentia)	2
Ichthyosis	3	3
Spina bifida	with hydrocephaly 2, with paralysis 1, others 2	5
Meningocele	3	3
Hand conditions	web 1-2 fingers, 2-3 fingers (2 cases), not specified 3, 6th finger or extra thumb 2, 4 fingers too large 1, congenitally contracted fingers 1 ...	10
Foot conditions	web 2-3 toes (4), 3-4 toes (2), 4-5 toes (2), unspecified 4, "deformed toes" 2, deformed foot 1, small toes 1, 3 toes incomplete 1 ...	17

TABLE V.—STIGMATA IN GROUP C.

		Total
Eye conditions ...	congenital cataract 2, blind 4, optic atrophy 1 ...	7
Ear conditions ...	asymmetry 5, deformed 1, accessory auricle 2 ...	8
Face conditions ...	asymmetry 6, deformed 1, hypertelorism 31, with or without epicanthus. Epicanthus 10 ...	41
Head	asymmetry 1	1
Hare-lip	1	1
Palate	partial cleft 3	3
Accessory nipple ...	2 right, 2 left	4
Heart	"congenital heart" 2	2
Hermaphroditism ...	1	1
Nævus	nævoid amentia 2	2
Albino	1	1
Hand conditions ...	webbed fingers 2, deformed thumb 2, index 1, deformed hands 1, 6th finger 1, small finger 1, synostosis of metacarpals 1	8
Foot conditions ...	webbed toes 5, long or short toes 15, deformed foot 1, 6th toe 1	22

Relation to mental deficiency as a whole.

Every writer on the subject states that anomalies of development, or stigmata of degeneration, occur much more frequently among the mentally abnormal than among the mentally normal, but the strange thing is that it is very difficult to find any numerical evidence for the statement.

The following are the few detailed figures that I have been able to find at present:—

Gradenigo found normal ears in only 56% of normal males and 66% of normal females, and gave the corresponding figures for the insane as 36 and 46, and for criminals as 28 and 54 [9]. In my series, in Group *C*, there were only 2% abnormal.

Auricular fistulæ were found 12 times in 2,000 cases by Urbantschitsch, and my series has none; auricular appendages were found by Warner in 33 out of 50,000 children [10]. My Group *C* would have shown 160 cases, and Groups *A* and *B* would have shown 20 if magnified to the same total, a much bigger ratio.

If cleft palate be considered, my Groups *A* and *B* show 4% and Group *C* only 0·5%. These figures compare with 0·5% in aments according to Langdon Down, 1·0% in idiots according to Ireland, none in nearly 2,000 feeble-minded according to Talbot, and 9 in 14,466 normal people according to Grenyer [9].

Lastly, Mitchell Bruce found accessory nipples in 11% of a group of 207 men and in 4% of 104 women [2]. Groups *A* and *B* have only a 12th of 1%.

It is a question what all these figures are worth. They are undoubtedly contradictory in their indications, and are open to the same criticism as those of my three groups—that they are the product of many different people working under different conditions and using different standards.

I offer figures for a good series of defectives, which is, perhaps, a useful contribution to the subject, but I hope shortly to examine a series of normal schoolchildren to compare them with my 600 defectives, and that should give help in settling this question.

May we take it that the consensus of opinion is probably right, and that there are more physical anomalies in mental defectives than in the mentally normal? But may we also make the reservation that the difference between the two is probably less marked than we have been given to believe?

If now we try to discover what reason may underlie this probable relationship between physical anomaly and mental deficiency, it is necessary to review the causes that have been suggested in explanation of the one and to see if there is any link with the supposed causes of the other.

Mall [11] had the opportunity of making a careful study of large numbers of embryos and he gives his conclusions, based on 1,000 pathological specimens. He decides against hereditary and germinal causes for the pathological conditions and favours environmental causes. He lays stress on faulty implantation of the ovum or on faulty nutrition through the chorion, and teaches that the result may be localized, as in the anomalies that have been described, or generalized to form monsters, and that this depends on the degree of localization or on the time of action of the nutritional defect. He would further explain the local developmental error by suggesting that there is a normal harmony or correlation of growth between all the parts, and that the nutritional defect, though a general influence, may cause a dissociation or disharmony in such correlation.

Ballantyne [10] explains some anomalies as due to amniotic adhesions, and Keith accepts this as the cause of certain superficial conditions, such as fistulæ about the face. In dealing with congenital malformations in this region he particularly blames morbid conditions of uterus or placenta, but also points out the strong familial and hereditary quality of some of these anomalies and their tendency to be grouped together.

J. Percy Good [12], on the other hand, denies the responsibility both of unhealthy chorion and of amniotic adhesions. Neither condition was present in his examination of a spina bifida in the neck region of a ferret embryo. He suggests that some echanical condition may result in irritation and inflammation, and believes that sp bifida may be caused by an extreme degree of spinal flexion, which causes distu nce of the growing parts and results in failure of completion of the structures the neural arch. He does however agree with Mall's dissociation theory.

In connection spina bifida it should be noted that this is one of the commonest results c orts at the production of experimental anomalies, by whatever method is employe Baldwin describes his method of treating frogs' eggs with ultra-violet light and claims that by his technique he can produce spina bifida in 90% of his attempts [13].

Turning now to the opposite extremities of the body, it is interesting to consider the arguments of Lewis and Embleton in their exhaustive study of the G. family [14]. Here in seven generations "split" or "lobster claw" hands or feet occurred in 44 out of 180 members. They give good reason for rejecting maternal impressions and acquired or extra-uterine lesions as satisfactory explanations of this deformity. They also reject atavism, and developmental arrest, and believe that the first of the

G. cases was due to the appearance, as a sport, of some quality which acted as a disturber of an inheritable factor which controls development of the extremities. It was not truly Mendelian in action.

Their objections to atavism are of interest. They rely on Bland-Sutton's dictum that atavistic structures do not belong to forms palæontologically remote or systematically far distant. Atavism therefore is a poor explanation of polydactyly, there being no ancestor of man with more than five fingers, nearer than ichthyosaurus. As some of the cases had polydactyly it would be unreasonable to invoke two explanations for the whole individual when one would be more likely to meet all the conditions. On the other hand Keith appears to accept a mechanism very like atavism. He gives the impression throughout his writing that he is satisfied with this explanation of a physical anomaly so long as he can be sure that somewhere in the phylogenetic history there is a similar condition, and this argument seems to cover the idea of arrest of development.

Another principle much favoured by Bland-Sutton, not denied by Keith, but not adopted by Lewis and Embleton, is that of dichotomy, which seems to be a satisfactory explanation of many conditions, from polydactyly to identical twins! If now we try to review these possible explanations of physical anomalies in order to correlate them with the causation of mental deficiency, it is hard to obtain any clear guidance. There is little agreement on the reality of operation of the various suggested causes, and it is not certain how many of the anomalies are worthy of classification as degenerative or as stigmata in the modern significance of the word. Some may be indications of advance rather than retreat in the march of evolution. No member of the G. family, for instance, showed any trace of mental deficiency [15], and it is well recognized that these anomalies can occur in people of the best biological quality. It may be noted that a number of explanations are environmental, whether by nutritional defect, faulty implantation, amniotic adhesions or mechanical difficulties. It might be thought that these would link up with those of the secondary types of mental deficiency which are due to intra-uterine conditions, but the parallel is not very certain. These causes seem to be invoked particularly to explain cleft-palate and hare-lip and spina bifida which, as has been shown, are not closely related with deficiency.

Arrest of development seems to be an adequate explanation of syndactyly, which is normal at the seventh week, and not incompatible with the probable cause of other anomalies of fingers and toes. It is also not incompatible with the strongly familial factor that is found in these conditions, for it is probable that it is an inheritable factor of some sort which determines these disorders of growth. It is noticeable that most of the anomalies that have been described have been produced by the eighth week of intra-uterine life, and takin is in association with the familial quality, it is not unreasonable to believe at the anomaly is ordained by some germinal quality, present before concept This is exactly parallel with the present idea of the causative factor in 80% o ntal defectives.

Reference to the tables will show that the physical ano es most frequently associated with mental deficiency are those of hands and and asymmetries and growth disorders of face, head and ears. Thus it appears t, in so far as there is a relationship between mental deficiency and physical a nalies, it is in the heritable or general sphere rather than in the environmental, and this is some slight confirmation of the primary or germinal theory of most mental deficiency.

There is still unsolved the question of the apparently small degree of correlation, and for the moment we are left with the suggestion already made, that a mental defective may be an example of a generalized state of impaired development in whom the only essential localized feature is inadequate cerebral structure. A somewhat similar, but not necessarily identical, mechanism may produce anomalies of a more localized nature in other parts, and these may occur in any individual, but

are rather more liable to occur in the mentally defective than in the mentally normal.

I have to express my thanks to Dr. James Nicoll, Medical Superintendent of the Fountain Hospital, for permission to make use of the clinical material and records of his hospital in the compilation of this paper. Further, I wish to state that the London County Council is in no way responsible for any of the views expressed.

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Section of Therapeutics and Pharmacology.

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Salyrgan in the Treatment of Heart Failure.

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MERCURY has long been used in the treatment of heart failure, but the use of the more complicated organic mercury compounds dates from the introduction of novasurol as a diuretic by Saxl [6] in 1920. Injected either intramuscularly or intravenously in the form of a 10% solution, in doses of ½ to 2 c.c., novasurol was found to produce a prompt diuresis of 3 to 6 litres in cases of œdema. Further clinical experience soon showed, however, that novasurol was liable to induce a severe degree of mercurial poisoning, and such complications as stomatitis, diarrhœa, hæmorrhagic colitis, proctitis, nephritis and hæmaturia, were reported, and fatalities occurred. According to Barker and O'Hare [1] mercurialism of some degree occurs in 25% of cases treated by novasurol. My personal experience with novasurol has been slight, as I abandoned it quickly owing to its toxicity.

Salyrgan was introduced later by a German firm, and the first reports on its clinical use as a diuretic appear to be those of Brunn [3] and Bernheim [2] in 1924. Salyrgan is a complex organic mercury compound of sodium-salicyl-allyl-amido-acetate, and contains 36% of mercury. Though it contains a slightly higher percentage of mercury than novasurol, it is far less toxic. It is put up for injection in a 10% solution and the dosage is the same as that of novasurol, namely ½ to 2 c.c

Pharmacology.—Without discussing in detail the theoretical mode of action of salyrgan and novasurol, it may be said that they are supposed to be "tissue diuretics," acting by diminishing the affinity of the tissue colloids for water and sodium chloride. Crawford and McIntosh [4] found that a dilution of the blood and an increase in chloride concentration preceded diuresis. The total chloride excreted in the urine is increased, but the urea is little affected. Others believe that salyrgan acts mainly on the kidneys, either directly or as part of a general vascular effect. Clinical experience lends support to this, as salyrgan fails, or is less effective, in pure renal œdema such as we find in nephrosis, and it appears that reasonably efficient renal function is essential for salyrgan diuresis. Both salyrgan and novasurol act better when combined with the administration of acid-producing salts such as ammonium nitrate or chloride, or calcium chloride. Recently Schelling and Tarr [7] have obtained equally good results by combining magnesium sulphate with salyrgan. They inject 15 c.c. of 50% magnesium sulphate with 2 c.c. of salyrgan and a small quantity of novocain deeply into the buttock. I have no experience with this method but I believe that intramuscular injections are best avoided.

It has been assumed that salyrgan has a less powerful diuretic action than novasurol, but this has been questioned by others, for instance by Grunke [5], and I think that salyrgan is often, though not always, the equal of novasurol and that, under similar conditions, both will prove effective.

Toxic effects.—Mercurialism never results from salyrgan in proper doses, as far as my own experience goes. I have never observed it in the course of several hundred injections, and Bernheim, in 1,000 injections, saw no toxic results. Others have had similar experience, and I know of no reported cases of mercurial poisoning from salyrgan. Two of my patients have had over 50 c.c. of salyrgan in eighteen months without ill-effect. For this reason, salyrgan should entirely replace novasurol as a diuretic.

Clinical experience.—Since first observing the excellent results of salyrgan in cardiac failure eighteen months ago, in Vienna, I have employed it regularly and

with increasing success as I gained experience with it. After a trial of intramuscular injections, given without any special regimen of fluid restriction, I found the intravenous method far superior in every way. Not only is the diuretic effect more powerful and more certain, but the unpleasant and painful complications which often follow gluteal injections are avoided. I give a first dose of 1 c.c., and then 2 c.c. doses at intervals of four days for as long as is required. The salyrgan solution should be diluted to 10 c.c. with sterile distilled water or saline, and all alcohol should be removed from the syringe. The injection should be given very slowly, taking several minutes altogether, and, after removing the needle from the vein, the arm should be elevated above heart level at once, so as to empty the vein. Given in this way I have not had a thrombosis of the vein, but if given undiluted, thrombosis is not uncommon. In one case thrombosis of the radial artery occurred, and I think that undiluted salyrgan must have leaked from the vein, around the wall of the artery, as the pulse only disappeared after several days.

In the treatment of severe cardiac failure by salyrgan, the following routine has proved best:—

(1) Give salyrgan intravenously; first dose 1 c.c., followed by 2 c.c. doses at intervals of four days.

(2) Give ammonium chloride by mouth in doses of 15 to 30 gr. thrice daily.

(3) Routine digitalis treatment should not be modified and full digitalization should be rapidly induced and maintained.

(4) Fluid restriction must be rigid. Usually the total fluid intake should be reduced to 20 to 30 oz. in twenty-four hours, and should never exceed 35 oz. I believe fluid restriction is the key to successful treatment by dehydration with salyrgan.

(5) If hydrothorax is present—and a unilateral right-sided hydrothorax is almost the rule in cases of gross heart failure requiring salyrgan—paracentesis should be performed, not more than 35 to 40 oz. being removed slowly at a single operation. It is not necessary to tap ascites.

(6) The patient should be weighed daily, as body weight is the best guide in judging the progress of dehydration treatment. Ambulatory cases are easily weighed, and any rapid gain in weight indicates fluid retention at once.

Used in this way, there is almost always a prompt diuresis of 100 to 200 oz. after the first doses, and a fall in weight of 14 to 20 lb. in the first week, and up to 40 to 50 lb. in a few weeks. The diuresis begins in one to two hours and may last forty-eight hours, but it is usually over in twenty-four hours.

Contra-indications.—Acute nephritis, or the presence of blood in the urine, must, at present, be regarded as an absolute contradiction to salyrgan. Albuminuria is no contradiction. Perhaps diarrhœa or colitis should entail caution. It has been stated that salyrgan predisposes to thrombosis, and therefore the presence of thrombosis anywhere should also entail caution.

Type of case.—I have records of my results from salyrgan in twenty-seven cases of cardiac failure of different types, as follows: rheumatic heart disease, eleven cases; hypertensive heart disease, seven cases; syphilitic heart disease, five cases; adherent pericardium (Pick's disease type), two cases; auricular flutter of undetermined origin, one case.

In only three of these cases did I fail to get satisfactory diuresis, and in all three the patients were moribund before receiving salyrgan.

It is not necessary to have œdema to obtain benefit from salyrgan dehydration, as fluid retention of several litres, or 10 to 12 lb. increase of body weight, may occur without œdema. If the liver is large, the lungs engorged, and the cervical veins filled abnormally, benefit may be obtained.

Salyrgan has one advantage over digitalis: it acts equally well in failure with normal rhythm as in failure with fibrillation. In syphilitic heart failure, salyrgan

should be, theoretically, the ideal drug, as it combats not only the failure but also its underlying cause. Though I have had good immediate results from salyrgan, the prognosis in syphilitic failure is so grave that lasting benefit is scarcely to be expected. Salyrgan cannot restore a damaged heart, but it can give to a patient with chronic failure great amelioration and, if diuretics are of any value at all, then it is unquestionably the best we possess at present, and should be the first choice.

Illustrative cases.—The following five cases may be cited as examples of the successful use of salyrgan :—

Case I.—Rheumatic heart disease ; mitral stenosis, auricular fibrillation, chronic congestive failure.

Female, aged 41. Heart first affected at age of 15, following rheumatic fever. Increasing breathlessness for fifteen years. When first seen she had been confined to bed for eight months, taking digitalis. Orthopnœa, cyanosis, œdema of back, thighs and abdominal wall; liver much enlarged ; right hydrothorax.

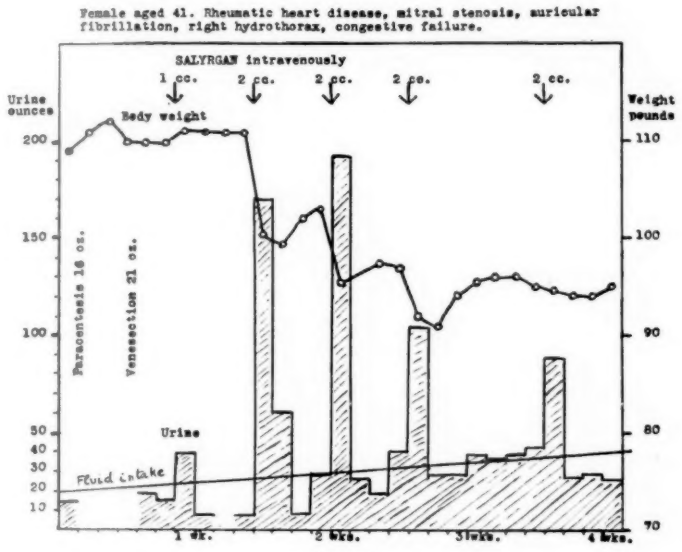

FIG. 1.

In this and subsequent figures are charted the daily output of urine, the body weight, and the salyrgan given.

Treatment.—After paracentesis and venesection, salyrgan injections combined with fluid restriction produced a maximum diuresis of 194 oz. in twenty-four hours, and a loss of 20 lb. in body weight in three weeks. Great improvement followed, and the patient is now able to get about free from œdema. (See fig. 1.)

Case II.—Hypertensive heart failure, with normal rhythm.

Male, aged 49. Admitted to hospital with severe congestive failure ; orthopnœa, gross œdema, congestion of lungs, and enlarged liver. Three months previously, severe pain in chest, probably anginal. Blood-pressure, 200/135 mm. ; gross pulsus alternans of 20 mm. ; heart greatly enlarged to left, gallop rhythm.

Treatment.—Venesection and digitalis, followed by salyrgan injections. Prompt diuresis up to 120 oz. in twenty-four hours ; loss of weight of 50 lb. in three weeks. Left hospital free from œdema and able to get about in comfort. (See fig. 2.)

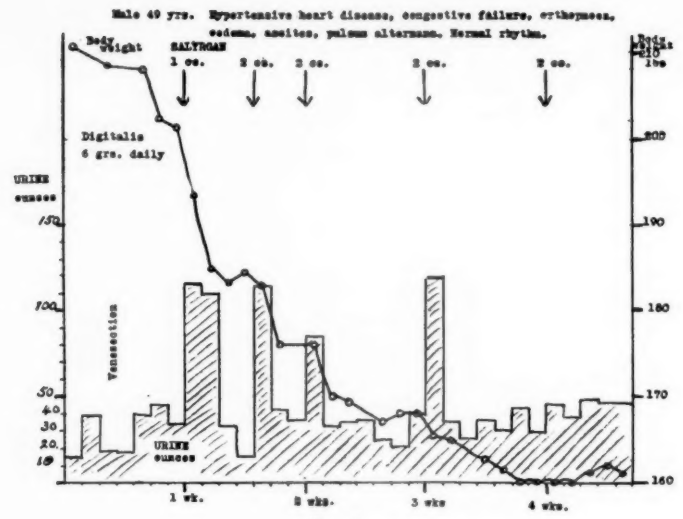

FIG. 2.

Case III.—Syphilitic and arteriosclerotic heart disease, hypertension, aortic incompetence, congestive failure with normal rhythm.

Male, aged 66. Under treatment for eighteen months with cardiac asthma, intermittent

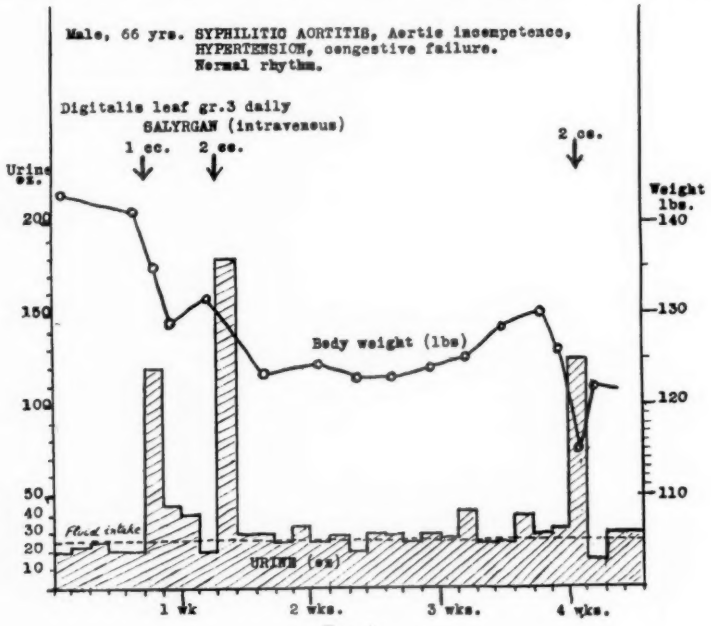

FIG. 3.

claudication, enlarged heart, and aortic incompetence; blood-pressure, 210/100 mm. Wassermann reaction, positive. Admitted to hospital with congestive failure and œdema; taking digitalis.

Treatment by salyrgan and fluid restriction produced diuresis up to 180 oz. in twenty-four hours, and fall in body weight of 20 lb. in two weeks. Great improvement but failure recurred later, and further salyrgan again removed œdema. (See fig. 3.)

Case IV.—Chronic adherent pericardium with calcification (Pick's disease).

Male, aged 36. Liver and spleen enlarged for many years, and calcification of pericardium discovered by X-ray examination. In bed two months with œdema of legs, thighs and back, and ascites; taking digitalis.

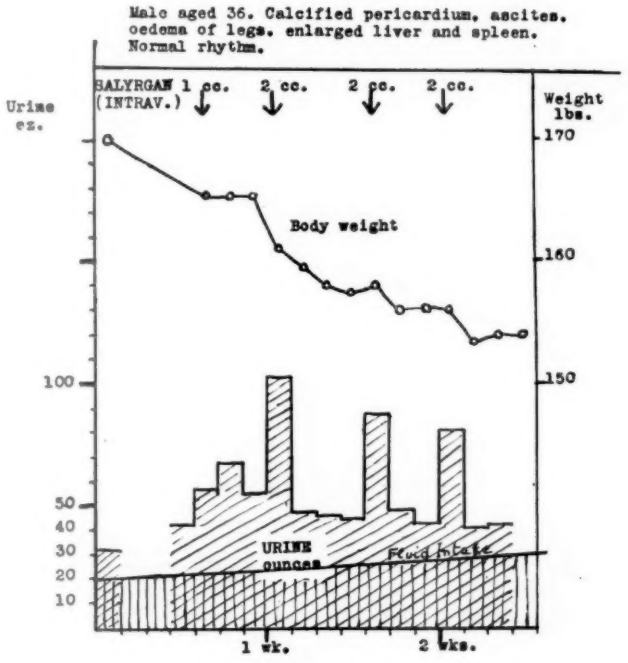

FIG. 4.

Treatment by salyrgan injections and fluid restriction produced a diuresis up to 102 oz. in twenty-four hours, and a loss of body weight of 16 lb. in two weeks. Considerable improvement, followed. (See fig. 4.)

Case V.—Rheumatic heart disease. Mitral and tricuspid stenosis, auricular fibrillation, congestive failure.

Female, aged 40. Rheumatic fever when aged 3. Breathless for many years, and for three months unable to get about owing to dyspnœa and œdema; deep cyanosis, liver enlarged and pulsating forcibly, jugular veins greatly distended and pulsating. Digitalis had already been given and was continued. Salyrgan injections and fluid restriction gave a prompt diuresis, and a loss of body weight of 38 lb. in four weeks. Improvement was great,

and the patient has now been getting about, free from gross failure, for eighteen months. Salyrgan injections have been given at weekly or fortnightly intervals, and if they are stopped the œdema reappears. In all, 75 c.c. of salyrgan given without any toxic effect. (See fig. 5.)

Female aged 40. Rheumatic heart disease. Mitral and tricuspid stenosis, auricular fibrillation, congestive failure, ascites.

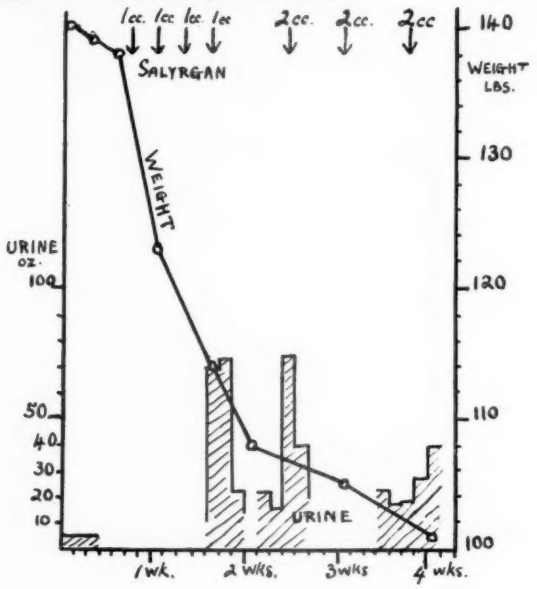

FIG. 5.

Summary.—Salyrgan may prove useful under the following conditions :—

(1) In gross congestive failure of recent onset, as an adjunct to digitalis it hastens recovery.

(2) In cases of chronic failure, when hepatic enlargement and œdema persist in spite of full digitalization, it will often banish œdema and add greatly to the comfort and efficiency of the patient. Weekly or fortnightly doses may be given to ambulatory cases, and should aim at keeping an optimum body weight.

(3) In cases of adherent pericardium with ascites, or of pericardial effusion with œdema of superior vena caval distribution.

[The paper was discussed by Dr. Strickland Goodall, Sir James Dundas-Grant, Dr. F. E. Loewy, Dr. Terence East and Dr. H. Gainsborough.]

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Section of Laryngology.

[*December* 5, 1930.]

Plastic Repair after Operations on the Upper Jaw.

By E. Musgrave Woodman, M.S.

(1) Principles in Avoidance of Deformity. (2) Plastic Repair of Deformity. (3) Dental Cosmetic Repair.

(1) *Avoidance of Deformity.*—Deformity after operations for malignant disease of the upper jaw should never take place, provided that cases are seen sufficiently early and that the operation is carried out along scientific and artistic lines.

The earliest description of this operation I have been able to find is by Richard Wiseman, Sergeant Surgeon to King Charles II, who, in 1671, described a patient with this condition in the following words:—

"A man, about 28 years of age, came out of the country with a cancer on his left cheek, stretching itself from the side of his nose, close under the lower eyelid to the external canthus, so making a compass downwards. It was broad in its basis, and rose capped like a sugar-loaf. The cancer threatened his eye with inflammation, and he hastened up and he importuned me to undertake it."

Any operation undertaken on such a patient is clearly destined to lead to severe deformity. When the soft tissues and skin of the cheek are invaded, deformity is inevitable, whether the operation is undertaken by the scalpel, by radium, or by diathermy.

It is remarkable how rarely the external parts of the nose itself are invaded, but when this takes place a new nose must be constructed.

The unhealthy, baggy swelling sometimes seen below the eyelid on the affected side must be avoided. The old transverse incision below the eyelid must be relinquished, and the method mentioned by Trotter, through the inferior fornix of the eye, should be used, or the one which the author introduced, and always uses, which commences in the eyebrow and extends down the side of the nose, the eye being temporarily displaced outwards.

A gap, due to failure to unite in the region of the inner side of the nose near the inner canthus of the eye, is particularly difficult to close, except by elaborate plastic repair. Union can best be attained by uniting the periosteum by a separate layer of buried catgut sutures and then suturing the skin very accurately by carefully placed silk sutures.

Dislocation of the eyeball must be guarded against. If possible the infra-orbital margin of bone should be retained; failing this, the suspensory ligament of the eye should be left. Even in the worst cases the eye can be saved by packing the cavity tightly with gauze soaked in bismuth, iodoform and saline (all sterilized), and held in position by a "Stent" temporary dental plate.

Perforation of the palate should not be regarded as a deformity. Increasing experience leads me more strongly than ever to teach that an opening for inspection should be made in the palate in every case; without this it is impossible to watch

the operation area effectively over the necessary period of time. This opening is controlled by a denture, which is held in position very effectively by two soft rubber extensions into the opening and enables the patient to speak and eat freely.

(2) *Plastic Repair of Post-Operative Deformity.* Nose.—The nose is frequently destroyed by the ravages of syphilis, tubercle, and war, but rarely by malignant disease.

Repair is undertaken readily by swinging a flap down from the forehead by the method introduced by Sir Harold Gillies, to whom I owe my interest in this subject. (Cases I and II.)

In the last case of the kind in which I have operated I deliberately took a portion of the hairy scalp at the end of the flap to implant on the side of the nose and then depilated it by X-rays; by so doing, a scar on the forehead was avoided. (Case III.)

Face.—A large opening in the cheek can be remedied by a swing of a tube graft from the chest to the malar region (monocle swing). This is the first operation. At a second, a portion of rib cartilage is inserted within the grafted tube, with its tip near the upper end. At a third operation the upper end of the tube is split and is laid across the opening, the inner skin layer lines the antrum, the outer forms the external covering, while the cartilage supports the bridge.

Much more difficult is the repair when the eye has gone as well. Attempts, in my hands, to lay a large fat tube across the face and fix it to the side of the remains of the nose (e.g., septum), and to leave an opening above to form a new orbital cavity, have proved a failure.

The fact is that the tube will not hold in this position and the only way I have found possible is to close the whole opening and fix the upper edge of the tube to the forehead, just below the eyebrows.

Mouth.—While I find the nose easy to repair, and the face more difficult, the mouth represents the summation of difficulty.

The case illustrated shows a man with an advanced growth of the upper and lower lips and angle of the mouth on the right side. The growth was effectually destroyed by diathermy and there has been no recurrence. As a necessary result of the operation, half his mouth was destroyed and the result was a facial expression which resembled a sardonic grin. Saliva dribbled constantly and food during mastication fell out of his mouth in lumps. (Case V.)

Repair was undertaken by a chest pedicle flap to the angle of the mouth, and then by a series of swings to form anew the upper and lower lips. At first the angle of the mouth on the right side formed a ring. This was rectified by a series of adjustments. The final result was a partial failure. The patient was able to retain his saliva and masticate his food, but his appearance remains to this day the reverse of pleasing. This case was one of extreme difficulty, owing to the mobility of the mouth and the frequent use of the parts in expression. A repair of the upper lip alone is comparatively easy and is undertaken along similar lines.

(3) *Dental Cosmetic Repair.*—The assistance of a skilled dental surgeon is of great value to the surgeon in carrying out the repair of the ravages of operation in his cases.

When a part of, or the entire half of, the palate has been removed, a temporary plate can be made and fitted in position a few hours after operation. This enables the patient to eat and swallow well and to retain the dressings in the cavity in a clean and healthy condition. Later on a more permanent plate with an intra-antral rubber extension serves to fill out the cheek and prevent that retraction and deformity which are liable to occur.

Again, when a large portion of the face has been removed and the patient, owing to age or disinclination, is unsuitable for surgical repair, a vulcanite shield can be exactly fitted in position and attached below to a dental plate, and externally coloured or even painted to match the face. Lastly, when the supports for the

nose have gone, but the external cutaneous covering remains, deformity can be entirely rectified by a vulcanite support fixed to the dental plate.

In conclusion, it is evident that the ravages of disease and its cure by operation can be ameliorated and rendered inconspicuous by the great art of plastic surgery, ably seconded by the improvement in mechanical dental technique available at the present day.

ILLUSTRATIVE CASES.

(I) W. P., female, aged 23.

Condition on admission.—Destruction of nose by lupus (now inactive). Right ala atrophied; left ala deficient; no nasal tip.

Plastic operations.—(1) (November 1926.) Forehead flap turned down, and sutured over end of nose. (2) (December 1926.) Tip of flap shaped to nose, and forehead pedicle returned.

(II) L. P., female, aged 23.

Condition on admission (1927).—Extensive destruction of alæ nasi and tip of nose by lupus, of twelve years' standing. Tissues anæmic and unhealthy.

Plastic operation.—(May 1927). Grafting of portions of whole thickness of skin from the abdominal wall in situ.

Result.—Aseptic necrosis and failure.

(III) Mrs. G., aged 62.

Condition on admission (June 1926).—Squamous epithelioma following rodent ulcer in left angle of orbit. Deep ulcerated hole, leading into nose, both upper and lower lids affected.

Operation.—Excision of growth; and diathermy; removal of the eye.

Plastic Operations.—(1) (May 1930.)—Isolation of forehead and scalp flap to make a pedicle. Turbinate swing to form support in nose for graft. Suture of end of flap in position over nose. (2) (June 1930). Return of pedicle flap to forehead. Depilation of flap on nose by X-rays.

(IV) S.B., female, aged 35.

Condition on admission (July 1924).—Large fungating mass filling whole of right orbit, and extending into right nostril; right eye destroyed.

Operation.—Whole of right maxilla, including orbital contents, removed.

Plastic operations (1) (July 1925.)—Tube graft isolated from abdominal wall and cartilage engrafted. (2) (January 1926.) Swing to right side of cheek. (3) (March 1926.) Swing across cavity to attach to side of nose. Attachment subsequently broke down. (4) (June 1926.) Swing across to attach to forehead above.

Eye socket to be made later.

(V) D. B., male, aged 46.

Condition on admission.—Large fungating carcinoma involving two-thirds of upper lip, right angle of mouth and half of lower lip.

Primary operation (August 1922.)—Diathermy and whole area removed right down to the mucous membrane covering the jaw and including the fornices.

Plastic operations.—(1) (August 1923). Tube graft isolated from thorax. (2) (September 1923.) Tube graft translated to neck. (3) (October 1923.) Tube graft to angle of mouth. (4) (June 1925.) Tube graft shaped round upper and lower lip areas.

Discussion.—Mr. T. P. KILNER said that as a surgeon dealing with cases only from the reconstructive point of view, he was full of admiration for Mr. Woodman, who tackled both removal and replacement. Such a combination had, however, one definite advantage: it allowed for the preparation of the ground for future plastic operations. The turning-in of skin edges and the suturing of skin to mucous membrane around the margins of a defect followed the practice of Sir Harold Gillies and himself.

He would like to hear something further about epilation of skin, for he had found no satisfactory means of destroying hair in skin areas intended for those in turned lining flaps so well illustrated in Mr. Colledge's cases (pp. 15, 16). X-rays, if used in sufficient doses to destroy hair follicles, destroyed also the vitality of the flaps.

He sympathized with Mr. Woodman in the disappointments he had experienced in attempting to reconstruct eyelids or lips by means of the tubed pedicle flap. The reconstructed parts almost always had the immobile thick appearance described. He recalled a case of extensive loss in the orbital region caused by the explosion of a Verey light in which, after closing-in the defect, he had attempted to reconstruct a cavity capable of holding an artificial eye. The attempt was abandoned because of the peculiar appearance given by the immobile masses representing the new eyelids. He contented himself with supplying the man with a simple shade to hide the absence of the eye.

He thought that Mr. Woodman was perhaps a little unnecessarily afraid of the scarring produced by the use of the forehead for these repairs. The forehead flap was ideal for this work, for it matched the surrounding face skin perfectly and had the additional advantage of being hairless when required for lining. Further, the secondary defect in the forehead lent itself admirably to free skin-grafting.

Mr. MUSGRAVE WOODMAN (in reply) said it was a mistake to suppose that he was afraid of using the skin of the forehead for flaps. When he had utilized the skin in the scalp region, his object had been to avoid a permanent scar. He agreed that forehead skin was ideal for the purpose. The surgeon who could prepare his cases with the view to subsequent plastic repair was at a great advantage over the man who only obtained them after the damage had been done.

Repair of Pharyngeal Defects after Operations for Removal of Malignant Tumours.

By LIONEL COLLEDGE, F.R.C.S.

THESE openings may occur as a complication after total removal of the larynx, or after lateral pharyngotomy, or they may be deliberately produced by removal of the larynx with either a portion or a complete segment of the pharynx, or by a lateral pharyngotomy in which such an amount of the lateral wall is removed that an opening is inevitable.

When such an opening occurs as a complication, the usual cause is wound infection, but defective nutrition of the skin may also produce one, either because the flaps have been designed with an insufficient blood supply, or because the skin has been damaged by radiation. To avoid wound infection, the mouth must be properly prepared and two or three weeks' interval must be allowed after the extraction of teeth. During the operation the wound must be kept free from pharyngeal mucus and the pharyngeal opening be closed securely. There is less liability to the formation of a pharyngostome after laryngectomy, if one large flap with its base at the hyoid bone is used, as the flap covers the suture line of the pharynx and the two lines of sutures in skin and pharynx do not coincide. No form of skin-flap, however, will compensate for defective technique. When X-rays have been used on the pharynx I think it is generally safer to stitch the pharynx to the skin and produce a pharyngostome. Healing is then obtained with less liability to sloughing, and the pharyngostome can be repaired later. I have not found that radium applied in needles, for intrinsic cancer of the larynx makes much difference to the healing of a subsequent laryngectomy. It is not necessary to refuse to operate on cases in which radiation has been used previously, but the fact must be taken into consideration in planning the operation. The bad results, however, which have made some surgeons refuse to operate on irradiated cases, teach their lesson, and my own experience in this connection is not very large. I do not think that irradiation is of any assistance either in eradicating the tumour surgically or in obtaining healing of the wound. I have not, however, had any cases in which the skin has been burned. The deep X-ray therapy has always been skilfully applied and the wounds have healed well after the plastic operations.

Concerning the actual closure of these pharyngostomes I have nothing fresh to say, but there are certain principles which must be faithfully observed if the opening is to be closed by a single act, for it is generally useless to freshen the edges and unite them unless the opening is quite small. It is also useless to slide a single flap across the opening, leaving an inner raw surface exposed to contamination by mucus and saliva. The gap must be closed by a double layer of tissue, which presents a lining of skin or mucous membrane facing inwards and of skin facing outwards. There may be sufficient mucous membrane to enable it to be detached from its junction with the skin, turned inwards and sutured, but it is usually necessary to dissect up skin flaps around the opening and turn them so that the epithelial surfaces look inwards. In this case the flaps of skin are completely cut off from their original blood supply, and sufficient interval—three or four months—must have elapsed for the skin to have acquired a fresh vascular connection in the new position. I use fine silk for deep sutures on account of its strength, inserting two rows and avoiding perforation of the epithelial surface by the stitch holes.

This leaves a large raw surface facing outwards, which must be covered by a flap taken from the immediate neighbourhood. The loose skin below the horizontal ramus of the lower jaw is usually available for this, but it may be taken wherever available, provided that the flap is thick, has a good blood supply which is not obstructed by rotating the pedicle, and is large enough to cover the surface without tension when stitched into position. In this way no raw surface is left exposed, the suture lines in the two layers do not coincide, and healing is obtained by first intention. There is no actual loss of skin in these cases, though a large amount may be required to replace the mucous membrane of the pharynx, and I have always found sufficient skin available locally without bringing it from a distance by a tubed pedicle.

The cases shown illustrate these points. If the skin to be turned inwards contains hair follicles, it is advisable to have it epilated before the operation, otherwise the hairs grow inside the pharynx and cause irritation.

Illustrative Cases.

(I) *Intrinsic carcinoma.*—Male, aged 55. Had been hoarse for about eight months. Sir StClair Thomson found the left cord fixed by a flat growth on the cord, bulging out the ventricle above and dipping into the subglottic area below. Growth extended backwards to tip of arytenoid and forwards into base of epiglottis and anterior end of opposite cord. He therefore referred the case for laryngectomy. As doubt had been raised concerning the diagnosis, a preliminary biopsy was performed to confirm the malignant character of the lesion.

March 14, 1930. Laryngectomy performed by raising a single flap with its base at the hyoid bone. The case shows how the situation of the opening into the pharynx is covered by this form of skin-flap.

(II) *Post-cricoid carcinoma.*—Female, aged 58. For five months had noticed some soreness in throat with cough and phlegm, but not much dysphagia and loss of weight. Voice normal. Œdema of pharynx behind arytenoids. Vocal cords movable. Thin woman with much pulsation at root of the neck and a "slapping" impulse thought to indicate an aortic lesion. No glands palpable.

April 12, 1930. Removal of larynx with a complete ring of lower pharynx and upper end of œsophagus, four inches long, the growth being 2½ in. long and extending round the circumference except for a narrow space on the posterior wall. Glands on both sides of neck cleared at same time. On account of the resulting defect in the pharynx and œsophagus after healing, the patient wore a Gluck's tube, through which she swallowed without leakage until

September 26. The front of the pharynx and œsophagus was then reconstructed from skin-flaps as shown in the diagrams. Normal swallowing was established in ten days without any leakage. The state of the patient is the same as after simple laryngectomy.

(III) *Carcinoma of pharynx.*—Female, aged 65. Frail physique. Had noticed irritation in throat for nine months, and recently some hoarseness and difficulty in swallowing, especially of saliva. Breathed badly at night. Epithelioma on right aryepiglottic fold extending on to lateral wall of pharynx and reaching almost to lower pole of right tonsil. Some glands palpable on right side of neck along the course of the internal jugular veins. Had auricular fibrillation and had been under treatment for heart failure. Seen by Mr. L. Graham Brown, who advised operation.

July 1, 1930.—Right side of neck cleared of glands, and growth removed by lateral pharyngotomy. Through gap remaining, epiglottis and opposite side of larynx could be seen.

October 10.—Opening closed by skin flaps. No leakage, and patient began to swallow normally four days afterwards.

(IV) *Carcinoma of pharynx.*—Male, aged 55. Voice altered for several months; lately dysphagia rapidly increasing; for ten days had been unable to swallow solid food. Ulcerating growth on left aryepiglottic fold and lateral wall of pharynx, also occupying entrance to pyriform fossa and reaching to mid-line on back of larynx. Thick, fleshy neck, with no palpable glands. Mouth cleared eight days before operation.

August 2, 1930.—Neck cleared of glands and growth removed by lateral pharyngotomy. The epithelioma was the size of a florin, so that the piece removed measured about 2 in. in diameter. Raw surface covered by turning-in a flap of skin from anterior part of wound. After healing, a long narrow cleft was left in lateral wall of pharynx. Dr. Hugh Gordon epilated the skin lining the pharynx where the mucous membrane had been replaced.

November 4.—Opening was closed by skin flaps. No leakage. Normal swallowing for soft solids established in nine days' time.

Discussion.—The PRESIDENT said he understood Mr. Colledge to say that in the case of one of his patients the swallowing was normal; did Mr. Colledge mean that statement to be taken literally, or were there reservations?

Mr. T. B. JOBSON asked where the line was drawn between operability and non-operability. Some of the cases now shown would have been regarded as inoperable a few years ago.

Mr. LAWSON WHALE asked—with regard to the case in which Mr. Colledge had removed the left side of the larynx and a large strip of the pharyngeal wall—how, since he lined that with a flap of skin turned inwards, he constructed the party-wall between what remained of the larynx and the pharynx?

Mr. MUSGRAVE WOODMAN asked whether Mr. Colledge had tried epilating the skin with X-rays before operation. He (the speaker) had a patient on whom he had performed this operation three years ago, and who periodically came up to have the beard cut as it grew in his pharynx when it reached the remainder of the epiglottis and tickled him.

Mr. LIONEL COLLEDGE, in reply to the President, said that the patient referred to now swallowed without any difficulty; the reason, he believed, was that the superior and middle constrictors were intact. The lower part of the inferior constrictor must have been totally removed. There was now no obstruction.

The question of operability scarcely came into this discussion. If the tumour could be removed, and if the resulting defect could be repaired by a plastic operation so as to give the patient a reasonably comfortable existence, he saw no reason to refrain from operating.

Mr. Lawson Whale had asked about re-forming the party-wall between pharynx and larynx. Mr. Trotter went rather further in that direction than he (the speaker) had attempted. It was difficult, because there must be a skin surface facing towards the larynx, and another facing towards the pharynx, and the first one was apt to prolapse forward and obstruct the larynx. Half of the larynx could easily be repaired, as in the three patients he demonstrated. If there was any large amount of septum between the pharynx and larynx to be removed, the procedure should be that adopted in Case II, in preference to an attempt at a plastic operation with a folded skin flap.

The hair growing inside the pharynx raised an important point, and he did not think X-ray epilation was suitable. Two patients sent to him by Mr. Mollison had both been treated by heavy doses of X-rays, but this had not hindered the progress of the tumour. They were

bare of hair when under the care of the speaker, and he treated them by an operation much on the lines of that in Case III, except that there was a strip of pharynx left at the back in both. The pharynx was repaired by turning up skin from the neck, and another piece of skin from the outside. Both grew hair in the pharynx later, and in one this caused some trouble. The other was not troubled by the hair at all. The hair therefore should be removed before the plastic operation. Dr. Gordon, of the Skin Department at St. George's Hospital, saw the fourth patient exhibited and thought X-rays would not be effective, and that radium would take a long time and perhaps would damage the skin; he therefore removed each hair separately by diathermy. He (the speaker) did not know what the ultimate result would be, but it was satisfactory so far, and he would try it again in other cases.

The Use of Carbon Dioxide in the Treatment of Vasomotor Rhinitis, Hay Fever and Asthma.

By Arthur F. Hurst, M.D.

In the summer of 1925 I visited Mont Dore, "la providence des asthmatiques," as it is known in France. It is one of the coldest and rainiest places in France, but it is situated 3,500 feet above sea-level, so that its altitude exerts a favourable influence on many visitors. Drinking the waters is regarded as an essential part of the treatment, but I cannot help doubting whether the trace of arsenic they contain can have any beneficial action. Walking round a room filled with the vapour of Mont Dore water at a temperature of 90° F. is the treatment upon which the physicians there lay most stress, on account of the "sédatif, décongestif, détersif, dérivatif, anticatarrhal et antispasmodique" action which the vapour is said to exert on the bronchi, and there is no doubt that it helps many asthmatics. A nasal douche of the gases derived from the Mont Dore water, consisting of over 99% of carbon dioxide, for from five to fifteen mniutes, is very commonly used. It produces a slight tingling sensation, and occasionally a burning feeling at the top of the head—probably when some of the gas enters the sinuses. Though it is claimed that the inhalation owes most of its success in the treatment of nasal catarrh to the fact that the gases are a natural product, I was so much impressed by the improvement which occurred in my own case that I thought a douche of ordinary carbon dioxide would be worth a trial at home. Before my visit I had been suffering from vasomotor rhinitis, and almost always had a running nose, with paroxysmal attacks of sneezing and rhinorrhœa. The one thing which Mont Dore did for me was to improve the condition of my nose.

For a long time I was unable to obtain a satisfactory apparatus, as the manufacturers would only supply the gas in enormous cylinders, and it proved impossible to make a generating plant which was safe as well as small. A year ago I saw Sir Francis Shipway give an anæsthetic, with which he mixed carbon dioxide from a small cylinder in order to make the patient breathe more deeply. This apparatus is now supplied with a rubber tube, at the end of which a nose-piece is attached (see fig.). The nose-piece is inserted in a glass of water, and the screw on the top of the apparatus is then very slowly turned in an anti-clockwise direction until a moderately rapid stream of small bubbles is seen to issue from the tube. The nose-piece is then dried and inserted into one nostril. The patient should breathe through his mouth and the gas should be allowed to flow into the nose without being actually inhaled.

In cases of vasomotor rhinitis the treatment should be given for from five to ten minutes up each nostril every morning. In hay fever this should be done throughout the hay-fever season, and in addition the gas should be used as often as necessary during the day immediately an attack threatens to begin and continued until it

passes off. For paroxysmal sneezing and nose-running the treatment should also be given immediately an attack begins. In cases of asthma which begin with an attack of this kind, the gas may prevent the attack from developing.

The treatment has proved of great value in a considerable number of cases of hay fever and other forms of paroxysmal rhinorrhœa and sneezing. It has often a

remarkable effect in vasomotor rhinitis, and is sometimes useful even when the condition is in part due to infection, though I do not suppose that it can exert any antiseptic action. Exactly how it works I do not know, but the action is certainly a direct one on the nasal mucous membrane and is quite distinct from that produced by the inhalation of carbon dioxide on the respiratory centre.

REFERENCE.

A. F. HURST, "The Treatment of Asthma at Mont Dore," *Guy's Hosp. Rep.*, 1925, lxxv, 58.

Discussion.—Dr. J. S. FRASER asked whether Dr. Hurst could give any explanation of how the carbon dioxide acted.

Mr. POPPER said he had been to Mont Dore, and he understood from a prominent doctor at the place that the irrigation with carbon dioxide was regarded as their sheet anchor in the treatment of nasal conditions.

Mr. CYRIL HORSFORD said that he had visited Bad Ems recently, and had been surprised and impressed by the new sanatorium, of which Dr. Diener was in charge. He was told that Dr. Diener was regarded as the authority in Germany on asthma, and he had been charged with investigating the subject. There a powder was vaporized, so that patients received the dried extract of Ems water in a volatilized form. Patients entered chambers at various pressures, and the treatment was said to have a marked effect on the asthma.

Dr. HURST (in reply) said he wished that he could explain the action of the carbon dioxide, but he was certain that the benefit was due to a local action on the nose; it was not a question of inhalation but of a direct action on the nasal mucous membrane.

THE PRESIDENT said that oxygen had had its boom, and now it appeared that carbon dioxide was having its turn.

Extrinsic Tumour in Right Posterior Mediastinum, causing Temporary Dysphagia.—HERBERT TILLEY, F.R.C.S.

Dr. K. T. G., aged 37, first complained of dysphagia June, 1930, followed shortly afterwards by pain in mid-sternal region on swallowing; noticed a zone of hyperæsthesia in same region. 11.7.30.—Sense of pain on swallowing solids or liquids. No physical signs in chest. 25.7.30.—X-ray examination showed obstruction in the mid-thoracic region caused by an oval tumour about the size of a hen's egg pressing on the wall of the gullet. 28.7.30.—Œsophagoscopy revealed narrowing of gullet but no lesion of the mucous membrane and a full-sized Jackson bougie passed easily without causing bleeding. Difficulty and pain on swallowing were much relieved and quite disappeared by 7.8.30; weight had increased by 14 lb. Present condition normal. (The patient's mother died from "intestinal tuberculosis," aged 36.)

X-ray examination.—"An oblique view of the chest shows a well-defined ovoid shadow in the posterior mediastinum at the level of 5th and 6th dorsal vertebræ. The barium swallow is held up temporarily just below the arch of the aorta and then passes down in a thin layer, outlining the opacity referred to above. This mass is apparently compressing the œsophagus from behind. The mass has not the typical appearance of a mass of glands and there is nothing in the dorsal spine to suggest a tubercular abscess. The appearance would be compatible with a benign tumour or cyst, since the smooth outline of the mass and the way it is pressing against the œsophagus (without apparently invading it) are against it being of a malignant nature." (A. J. Peake for Dr. Salmond.)

The patient was in the care of Dr. Batty Shaw (University College Hospital), who sent him to me for œsophagoscopy.

It is possible that the obstruction of the œsophagus was caused by a temporary enlargement of a lymphatic gland outside the œsophagus. Such temporary enlargement may have been due to septic infection in the neighbourhood, but of this there was no evidence. Or it might have been that the temporary enlargement was of the same order as that of other glands in lymphadenoma of the Pel-Ebstein variety, but against this was the absence of other evidence of lymphadenoma and of recurrent febrile attacks.

The last and most probable explanation is that the enlarged gland was an example of scrofula. Ulceration of a tuberculous gland through the œsophageal wall has been described. In the present case the pressure exerted by the scrofulous gland was not sufficient to cause ulceration.

"The enlargement of glands from scrofula has now received a measure of explanation at the hands of Ranke. In this case an ordinary radiogram of the chest has revealed the presence of a 'primary complex' which is the first tuberculous lesion of the lung and associated glands, occurring in infancy. It is common in young adult life for blood-strewn reinfection to originate from the glandular part of the primary complex: if at the time of this reinfection an œsophageal gland is reinfected and at the same time is in the second state of allergy described by Ranke, then an exuberant reaction takes place and the gland undergoes marked and sometimes rapid enlargement, as in other examples of scrofula, the subsidence of such swollen glands may be fairly rapid or may take many months." (B.S.)

Discussion.—Mr. T. B. JOBSON suggested the possibility of this being angio-neurotic œdema. Such cases had been described—one by Chevalier Jackson not long ago. In this case the obstruction was very evanescent. There was no other evidence of scrofula.

Mr. TILLEY (in reply) said he thought that Dr. Chevalier Jackson's cases were those in which the mucous membrane of the gullet was affected. In this case there was no swelling of the mucous membrane, only a pressure inwards from without, and bougies passed without any difficulty.

Tuberculosis of the Larynx simulating Cancer.—GEORGE W. DAWSON, F.R.C.S.I.

Patient a man aged 56, had had aphonia 2 months. Loss of weight 21 lb. Morning cough.

Larynx.—Considerable swelling of left false cord and a greyish swelling of anterior portion of left vocal cord; slight œdema of arytenoids. No temperature, and no tubercle bacilli found.

Treatment.—Sanatorium $2\frac{1}{2}$ months; silence, light and galvano-cautery. The galvano-cautery was applied five times but only after the general condition had been improved by the sanatorium treatment. The swelling has completely disappeared; the patient has recovered his voice and weight, and has returned to work after 14 months' treatment.

Discussion.—Sir STCLAIR THOMSON said that there were one or two useful general principles to be deduced from this case. He had seen the patient when he was in the sanatorium. The condition in the larynx was of the type often mistaken for malignant disease. As to tuberculosis, Mr. Dawson had examined the patient for that before he went to the sanatorium, and neither before nor during his stay there were tubercle bacilli found in his sputum. The diagnosis was made on the clinical appearance; the man had but little loss of weight, and skiagrams showed only a trifling condition at one apex, such as was found in a large number of people. This point of the absence of tubercle bacilli had been brought home to him (Sir StClair) in the last few days by the report of a case which he had seen in consultation, that of a middle-aged man, who had some dysphagia, and (showing that the laryngologist had not yet entirely come into his own) had had a laparotomy performed to discover why he could not swallow. When he came he had a typical tuberculous epiglottis, and as he had seemed fairly well two months before, and had no bacilli in his sputum, it was hoped that the case might be favourable. But the condition assumed a miliary character, there were large excursions of temperature, and the patient died. Yet he had never had tubercle bacilli in his sputum.

He (the speaker) had seen a fair number of such cases; one in a doctor from the West Coast of Africa, who was said to have malignant disease of the tonsil. He had entered a sanatorium, and had died within two months, with a hectic temperature and miliary tuberculosis, yet tubercle bacilli had never been found in his sputum. Another case was that of a Cambridge Blue in Ceylon, where his tonsils were excised, it not being realized that his dysphagia was due to tubercle. He returned to this country, and he (Sir StClair) had sent him to a sanatorium, where he had died within a few weeks, without having shown tubercle bacilli in the sputum, though they had been recovered from the fæces.

Most middle-aged patients who contracted tuberculosis of the larynx did well, if they were treated seriously. They composed a large number of the people going about with a mixed diagnosis of pachydermia and chronic bronchitis. They did well if they entered sanatoria, but if they were neglected they were apt to relapse, and if they relapsed they seldom recovered.

Mr. H. V. FORSTER said he had recently had a surprise in such a case, that of a man aged 60 who had always led an open-air life. Neither he nor his doctor had suspected tuberculosis. He had in the anterior commissure of the larynx, more on the right cord than on the left, a neatly defined growth. A senior colleague agreed that it was probably an epithelioma, but advised biopsy. The report on the piece removed by the indirect method stated that though for the most part the epithelial surface was intact, it was in one place ulcerated, and immediately subjacent were several typical tuberculous giant-celled systems, but there was no evidence of epithelioma. A skiagram showed definite phthisis of the right apex, and an indefinite mottling of the left.

Mr. DAWSON (in reply) said that the patient had never showed an increase of temperature; there were no tubercle bacilli and no cough, but there was complete loss of voice and a large swelling in the larynx. He regarded the case as one of primary tuberculosis of the larynx. It was generally contended that in tuberculosis of the larynx the lung was also infected, but he did not see why the larynx should not be primarily infected with tubercle.

Erythematous Patch on Soft Palate. ? Pre-carcinoma. — Sir JAMES DUNDAS-GRANT, K.B.E., M.D.

Patient, middle-aged man, complaining of pain in the throat was anxious as to the possibility of cancer, his wife having recently died from "cancer of the throat." There is a vascular erythematous patch occupying the right half of the palate. He smokes a good deal but there is uncertainty as to his holding the pipe invariably in the same side of the mouth. I have seen another case, almost identical in appearance, in which epithelioma developed within a year.

At the last meeting we were discussing pre-cancerous conditions, and we saw many chronic inflammatory conditions of the larynx but only one case in which cancer had developed. This patient has the decayed stump of a tooth, and possibly the removal of this local source of sepsis may cure him.

Congenital Syphilis. Deformity of Nose. Eruption of Teeth into Nose.—T. A. CLARKE, M.D.

C. P., a girl, aged 6 years.

Deformity of external nose, and loss of cartilaginous and bony septum. A tooth is seen projecting into the floor of the left nasal vestibule.

History.—The deformation of the nose and loss of the septum occurred twelve months ago. In July, 1930, an incisor tooth was removed, with some dead bone, from the nasal cavity and some weeks later another tooth was extruded from the nose. A third tooth was extruded from the nose a few days ago and it is a fourth tooth which is now seen in process of eruption.

The mother's Wassermann reaction is strongly positive.

The case is shown because of the rarity of the dental condition, but there is the further interest that it will be ten years before one can do a permanent plastic operation; meantime, should one be satisfied with a nasal prop to keep the right ala from collapsing?

Discussion.—Dr. W. JOBSON HORNE thought the probability of congenital syphilis being the cause of the condition might be overstated. He regarded it as a congenital malformation.

Mr. W. A. MILL said that about two years ago a similar case was shown by Mr. Mollison, in which a tooth had erupted into the nasal cavity. There was no suggestion of syphilis in that patient. The tooth had caused an atrophic rhinitis and perforation of the septum.

Bleeding Polypus of the Nose.—N. ASHERSON, F.R.C.S.

Patient, female, aged 40.

Had profuse epistaxis from the left nostril, spontaneous in onset, arterial in character and continuous. It arose from a granulation, the size of a match head, situated in the floor of the nose, just deep to the vestibule. After much trouble the flow was successfully stemmed. When the patient was seen four weeks later, the hæmorrhage had not recurred, and on inspection a hemispherical, blackish sessile swelling the size of a bean was detected. The surface was glistening and the tumour bled on touching. It was tense and resembled a sarcoma.

A skiagram showed the bone in the floor of the nose to be intact. The antrum was not involved. The inferior turbinate and the septum were normal.

After a week's interval the tumour presented a fleshy pale pink flabby appearance, similar to that of ordinary granulation tissue. It was snared off and bleeding was profuse, requiring the pressure of a pack to control it.

On section the tumour was found to be a bleeding polypus, that is to say, a hæmangioma. Dr. Scott Williamson, who examined it, reported as follows:—

"The tumour mass is made up of a very loose fibrous tissue banding a multitude of capillary blood and lymph spaces. It is essentially a plexiform angioma. The fibrous tissue is of a very embryonal type with few fibres. The surface is covered by an attenuated stratified epithelium."

The unusual features of the tumour are its origin from the floor of the nose and its altered appearance from time to time.

Dr. JOBSON HORNE said that the term "bleeding polypus" was misleading, and should be discontinued, both on pathological and clinical grounds. The term angioma would be more accurately descriptive of the condition.

FURTHER REPORT OF CASE PREVIOUSLY SHOWN.

Epithelioma of Vocal Cord treated by Thyrotomy in November, 1923 (shown April 4, 1924).[1]—Sir JAMES DUNDAS-GRANT, K.B.E., M.D.

The disease occupied the whole length of the right vocal cord and extended well into the anterior commissure.

In accordance with Chevalier Jackson's recommendation, the thyroid cartilage was divided from without inwards by means of a saw, and the soft parts were freely detached on both sides of the commissure before being divided. The whole of the right vocal cord and a considerable portion of the left one were cleared out. There was no difficulty in swallowing. The voice is rough but is very useful.

1 *Proceedings*, 1924, xvii (Sect. Laryng. 54).

Section of Odontology.

President—Mr. C. SCHELLING, L.D.S.E.

[*November* 24, 1930.]

The Teeth and the Stomach.

By ARTHUR F. HURST, M.D., F.R.C.P.

THE normal activity of the small intestine, in which the greater part of the digestion and the whole of the absorption of food take place, is of such fundamental importance to the body as a whole, that we are fortunate in possessing a double line of defence to protect it from unsuitable and improperly prepared food and drink and from infection. The first is the mouth and the second is the stomach. In the mouth food and drink are brought to the body temperature, while chemical irritants are diluted and hard particles are softened by the saliva. Lumps of food are broken up and brought into intimate contact with the saliva by chewing. A man, who is the fortunate owner of good teeth and sufficient leisure to use them, need therefore swallow nothing until its mechanical, chemical and thermal properties have been so altered that it will cause no irritation when it comes into contact with the delicate mucous membrane of the stomach.

Though the majority of people are provided with a first line of defence which is potentially adequate, comparatively few make sufficiently good use of it. Food is too often bolted without being adequately chewed, with the result that the gastric mucous membrane is daily subjected to mechanical, chemical and thermal irritation. In addition to this, if pyorrhœa alveolaris, tonsillitis or sinusitis is present, infected material is constantly swallowed.

Under these conditions the gastric juice dilutes chemical irritants, and very hot and very cold food and drink are quickly brought to the body temperature. The gastric juice dissolves connective tissues, so that chunks of meat gradually break into fine particles, and it softens, though it does not break up, lumps of unchewed carbohydrate food. Peristalsis in the distal half of the stomach brings the food to the pyloric sphincter, which remains temporarily closed if the food is insufficiently prepared, so that a churning process results which does its inadequate best to perform the functions which the teeth should have carried out. Lastly, the free hydrochloric acid of the gastric juice is a most efficient germicide and rapidly destroys the streptococci swallowed from the mouth, throat and nose, as well as most of the organisms present in contaminated food and drink. Thus, in most normal individuals the second line of defence proves adequate, even when the individual does not trouble to use his first line of defence or when the first line is imperfect. Consequently, with a normal stomach the small intestine is never subjected to thermal irritation, rarely to chemical irritation, and only to mechanical irritation if the bolting of food is exceptionally gross in character, and few, if any, bacteria succeed in passing the antiseptic barrier formed by the acid gastric juice.

Bennett and Ryle found that 10 per cent. of healthy students had a sufficiently high gastric acidity to deserve the designation of hyperchlorhydria and 10 per cent. had hypochlorhydria or achlorhydria. These variations are constitutional in origin

1 Read in the absence of Dr. A. F. Hurst owing to illness, by Dr. J. F. Venables.

and are examples of the physiological variations from the average which are so frequently found in perfectly normal people. When the stomach is ill-used as a result of deficient activity of the first line of defence, it is unlikely to suffer greatly unless its owner is one of the 10 per cent. in whom less than the average amount of gastric juice is secreted. The diluting, softening and breaking up of chemical and mechanical irritants is deficient, and the mucous membrane consequently becomes more and more damaged, until eventually chronic gastritis develops. The excess of mucus secreted to protect the mucous membrane then forms a thick adherent coating which blocks the mouths of the secreting tubules, so that little or none of the gastric juice reaches the lumen of the stomach. The result is that the hypochlorhydria gives place to achlorhydria.

Bennett and Ryle found that 4 per cent. of healthy students had achlorhydria; in most if not all of these the achlorhydria was due to a constitutional or inborn error of secretion—true achylia gastrica. About 12 per cent. of our patients at New Lodge Clinic have achlorhydria. In at least half of these it is acquired and the result of chronic gastritis, which can be cured by appropriate treatment so that the normal gastric secretion returns.

In achlorhydria, whether due to constitutional achylia gastrica or secondary to chronic gastritis, the absence of gastric juice renders the mucous membrane of the stomach very vulnerable to every kind of irritation, although it is protected to some extent if excessive mucus is secreted. The second line of defence is lost, with the result that the small intestine is irritated in exactly the same way as the stomach, so that duodenitis and enteritis develop in addition to the gastritis. Swallowed bacteria now flourish in the alkaline contents of the stomach and may invade its mucous membrane. Owing to the absence of the acid barrier normally offered by the gastric juice they pass into the duodenum, which therefore becomes infected. My colleague, Dr. F. A. Knott, has shown that the increased alkalinity of the intestinal contents at the same time allows bacteria which are normally confined to the colon, to ascend the small intestine as far as the duodenum and even the stomach, both of which now frequently contain streptococci from the mouth and colon bacilli from the large intestine.

This infection is the chief, though probably not the only reason why achlorhydria is so frequently associated with various diseases. It is always present in Addison's (so-called "pernicious") anæmia and in subacute combined degeneration of the spinal cord. It is the commonest cause of chronic diarrhœa, and an ascending infection of the appendix and gall-bladder accounts for its presence in 33% of cases of chronic appendicitis and 50% of chronic cholecystitis and gall-stones respectively. It is found in about 25% of cases of rheumatoid arthritis, and is more common in subjects of asthma and exophthalmic goitre than in normal people. Achlorhydria is also a very important predisposing cause of intestinal infections, such as typhoid and paratyphoid fever, bacillary and amœbic dysentery, and cholera, and its presence is a constant source of danger to residents in tropical countries.

Pyorrhœa alveolaris and, to a less extent, an inadequate chewing surface, thus play important parts directly in the pathogenesis of chronic gastritis and achlorhydria, and indirectly in that of a large number of secondary diseases.

I should now like to draw attention to the glossitis, which William Hunter first described thirty years ago as frequently present in Addison's anæmia, and which we now know to be equally common in the associated disease of the nervous system—subacute combined degeneration of the spinal cord. It is very rare in the absence of achlorhydria and may occur with it before any change has taken place in the blood or the nervous system, either or both of which may subsequently develop. I am speaking about it here, because many patients when they have a sore tongue, naturally think that the soreness may be due to their teeth, and their doctors may form the same opinion, whereas it is really the third constituent

of that remarkable symptom-complex—Addison's anæmia, subacute combined degeneration, Hunterian glossitis—of which achlorhydria is the essential predisposing cause. If dental surgeons become familiar with the appearance of the tongue in this condition, they will, I think, not infrequently have the opportunity of advising patients to have a test-meal and a blood examination, with the result that a rational prophylaxis of these serious diseases may be instituted. In the non-acute stage the tongue is clean and at first sight might be regarded as normal, but closer inspection shows that all the filiform papillæ have disappeared.

The 10 per cent. of people with hyperchlorhydria have such an abundant flow of strong gastric juice that they are better protected from ordinary gastritis than the average individual. Consequently the passage into the blood of bacteria and toxins from infected dental roots and from the ulcerated surface in pyorrhœa alveolaris and their excretion by the gastric mucous membrane are of more importance than the swallowing of bacteria, which are rapidly destroyed by the abundant acid present. According to Rosenow it is possible to isolate from the teeth of most patients with gastric and duodenal ulcer, a streptococcus which has a specific affinity for the gastric and duodenal mucous membrane and consequently produces ulcers in the majority of animals inoculated with it. Rosenow's work has received very little confirmation, but there is a good deal of clinical evidence which suggests that dental infection of all kinds is an important factor in the pathogenesis of gastric and duodenal ulcer in individuals predisposed by a constitutional tendency to hyperchlorhydria. I am convinced that the thorough treatment of pyorrhœa alveolaris and the extraction of teeth with infected roots are not only important for the successful treatment of an ulcer, but play a still more important part in the prevention of recurrences after healing has taken place. It should be remembered too that in the usual methods of medical treatment for ulcer the gastric contents are more or less completely neutralized throughout the day. If pyorrhœa is present, swallowed bacteria will have an unusual opportunity of invading the ulcer from the surface and may thus delay its healing. Though it is rarely wise to carry out very radical measures in the early stage of medical treatment, a good deal can be done by careful dental hygiene, to prevent the swallowing of infected material. Any teeth which require extraction should be taken out as soon as all occult blood has disappeared from the stools, whilst the patient is still on a strict diet. Care should be taken to prevent swallowing of blood and infected material; if this cannot be prevented, the stomach should be washed out as soon as possible after the extractions, as otherwise an acute exacerbation of the ulcer may occur. The thorough non-operative treatment of pyorrhœa is best postponed until the patient is convalescent. He should be told to have his teeth attended to regularly every three months, as the tendency to ulcer is constitutional and never disappears.

It is worth mentioning here that there is a great deal of evidence which indicates that cancer of the stomach is never a primary disease, but is always secondary to either chronic gastritis, or less frequently, to chronic gastric ulcer, so that the prevention and treatment of these conditions may be regarded as an indirect method of preventing cancer.

Finally I should like to say a few words about dental sepsis and abdominal operations. Whenever possible an operation on the alimentary tract should be postponed until any pyorrhœa alveolaris which may be present has been at any rate temporarily overcome. The exposure of the peritoneum in an abdominal operation results in reflex inhibition of the motor and secretory functions of the alimentary tract. The result is that temporary achlorhydria is produced, so that oral streptococci are not destroyed when they are swallowed, and the suture line may become infected. This is probably an important cause of those cases of gastro-jejunal ulcer which develop immediately after the performance of gastro-jejunostomy.

I hope I have said sufficient to convince you how much you, as dental surgeons, can do by dental treatment and dental prophylaxis, and by educating your patients,

to prevent the development of gastric disease and the many disorders in other parts of the body to which it may give rise.

Discussion.—Mr. J. G. TURNER said that he would like to know what value was placed on the mastication of meat? Were human beings fitted to swallow any mass that would comfortably go down, or was it necessary to masticate? He believed that of all foods, meat needed the least mastication, and it appeared from the paper that the stodgy carbohydrates were those that required the most insalivation. Also, was it possible that bacteria actually passed into the stomach, although at feeding time there might be a normal acid gastric juice, e.g., in a child or adult suffering from adenoids with a large amount of foul, purulent secretion, did the passage into the stomach excite any gastric juice at all, or did it rather tend to inhibit the secretion, and would that open the way to allow bacteria to pass into the small intestine. Dr. Izod Bennett had said that recurrence after operation for duodenal ulcer was largely a matter of dental sepsis, and could be prevented by total extraction of the teeth.

Dr. E. STOLKIND said that in America life assurance companies, in arranging premiums, took into account the number of healthy teeth a person possessed. Every healthy tooth was valued at £200, and the more healthy teeth there were the longer was the expectation of life and the less the premium. Life assurance companies in the United States saw the connection between a healthy mouth and good digestion. Similar conditions obtained in Germany, where the health insurance authorities placed a value on the teeth as necessary for general good health. Apart from that, there was no comparison between the appearance of artificial teeth and natural teeth. There was a popular saying that good mastication was half digestion. Thoroughly masticated food was reduced mechanically to small particles and mixed with saliva which partly digested the starchy food, thus lightening the work of the stomach. Good mastication of hard food cleaned the teeth and tongue. Among the peasants of Russia the cleaning of teeth was unknown, but he had found their teeth as a rule to be of good quality. Their rye bread, raw cabbage and other foods required thorough mastication, and that, in his opinion, played a great part in the good condition of their teeth.

That the mere taking in of food caused a flow of gastric juice was shown by Pavlov. ("Dry food, even seen at a distance, promotes a copious flow of saliva"). Beaumont, Richet, Cade, Latarjet, Bickel, Katznelson, and Carlson had made observations on human beings with gastric fistulæ, with or without stricture of the œsophagus, and had confirmed Pavlov's findings.

In large towns people had lost the habit of mastication. They had no time. The food was prepared accordingly and was softened and rendered easy to swallow without mastication. Soft meat, fish, eggs, bananas and cooked fruit were substituted for raw apples, crusty bread and other hard foods, which were also useful in promoting the action of the bowels. Prolonged mastication, such as advocated by Fletcher and others was, however, superfluous. Thorough mastication carried out by good teeth was helpful in cases of diseased gastro-intestinal tract. Loss of appetite was sometimes associated with bad teeth. Artificial teeth could never replace natural teeth as regards efficiency in mastication. Those who possessed artificial teeth usually had to be careful in the choice of suitable food.

In patients seen in hospital a large proportion of artificial sets were badly made. There had been experiments on a vast scale in both England and America in the wholesale extraction of all the teeth. In this connection he might draw attention to the numbers of people who, after extraction of all their teeth, had resorted for years to the use of their gums. In many cases patients had been unable to use artificial teeth on account of the difficulty in wearing them. In spite of that, those under his observation for the past ten years, both in hospital and in private practice, were free from diseases of the stomach and intestine, thus indicating the adaptability of the human digestive system. He would quote two illustrative cases:

(I) A woman, aged 60. In 1920, before seeing him, she had had all her teeth extracted —though the dentist had found them in good condition—by her doctor's advice, because she had suffered from asthmatic attacks. She had not improved, but had become worse. Under the treatment for asthma, which he (Dr. Stolkind) had prescribed, she became free from attacks. She used her artificial teeth only as an ornament, and removed them for eating purposes. During the ten years she had been under his observation there had been no symptoms or signs of disease of the digestive system.

(II) A man, aged 58, suffering from polycythæmia vera, had been under his (Dr. Stolkind's) observation since 1921. All his teeth, though in good condition, had been removed on the advice of a doctor, who thought that procedure would bring about a cure. Naturally the patient did not improve. For the past ten years he had eaten without teeth, and there had been no digestive trouble.

There were thousands of such cases, and they afforded opportunities for a very necessary investigation as to the effect of lack of teeth on the digestive system. So far there was no scientific proof that diseased teeth or absence of teeth produced disease of the digestive system.[1] There was no argument, however, in favour of the ruthless extraction of the complete set of teeth such as was still practised in England.

Mr. H. H. KENSHOLE said that he understood Mr. Turner to have asked whether the degree of acidity of the gastric secretion remained constant or whether possibly the acidity was most marked at the ingestion of a meal, and during the intervening periods there might be a hypochlorhydria or even achlorhydria, which would permit of the passage of foul infected material from the mouth to the duodenum. There was undoubtedly a variation in the acidity of the secretion, and this led to the consideration of the alkaline and acid tides of the blood during the periods of ingestion and early digestion, and of late digestion and resting state respectively. He (the speaker) wondered, therefore, whether those people who showed hypochlorhydria or achlorhydria had been found to have, clinically, a relative alkalosis of the blood—such patients being said by Broderick to be essentially susceptible to periodontal disease—and, conversely, whether the hyperchlorhydrics had been found to be essentially persons of an acidotic type.

Mr. H. P. BAYLIS said that, with reference to the conditions of hyperchlorhydria and hypochlorhydria which had been described, it would be interesting to know if these were associated with any definite dental clinical picture and if they had any corresponding equivalent in the degree of acidity of the saliva.

Mr. S. A. RIDDETT said he would like to know the frequency with which the dentist might expect to find the complete syndrome (namely achlorhydria, glossitis and Addison's disease) present, among the patients seen in ordinary private practice.

Dr. VENABLES (in reply) said that with regard to the value of mastication of the different articles of food, that of meat was by far the least important. In the examination of vomited material it was rare, if the food had been in the stomach any length of time, to find any residue of meat that could act as an irritant, whereas there would probably be found large quantities of unaltered carbohydrate food. As to the question whether bacteria actually passed through the stomach into the duodenum, the contents of the duodenum were always sterile in people who had plenty of free acid in their stomachs. In his experience there was no dental picture to be associated with achlorhydria, except, of course, in those cases in which pus exuded from the mouth. With regard to the question of dead teeth acting as a focus of infection in cases of duodenal ulcer, extraction had been carried out after evidence that the ulcer had healed. His own experience of vaccines was not encouraging; they had been tried, but he had not been convinced that any material benefit had resulted so far as the ulcer was concerned.

[1] Stolkind, *Proc. Roy. Soc. Med.*, 1926, xix, 20; 1928, xxi, 81; 1930, xxiii, 1166.

Section of Ophthalmology.

CASES SHOWN AT A MEETING HELD AT THE CENTRAL LONDON OPHTHALMIC HOSPITAL, ON DECEMBER 12, 1930.

Iris Inclusion Operation for Glaucoma.—M. S. MAYOU, F.R.C.S.

F. M., female, aged 66.

History.—Rise in tension, right eye, March, 1928. Right trephine operation. Vision: Right eye, hand movements; left eye, $\frac{6}{18}$ with − 3 sph. Rise in tension, left eye, July, 1930. Discs cupped; corneal tags.

Decrease in nasal field. Extension of blind spot.

Operation, September, 1930. Left iris inclusion with small peripheral iridectomy.

The tension seems to be satisfactory, though there is no bleb over the operation wound. The procedure was as follows: First, I made a keratome incision and pushed the iris inwards, so as to create an irido-dialysis, then I pulled it outwards and made two snips in the iris, removing the tag, and leaving the angle of the iris caught in the wound.

Discussion.—Mr. GAYER MORGAN asked whether Mr. Mayou raised up the conjunctiva in order to make as large a flap as possible, or entered in straight at the limbus.

Mr. MAYOU, in reply, said that he raised a small flap of conjunctiva with the keratome before entering the limbus.

Tumour of Optic Nerve (?) with Sudden Hæmorrhage into it.—A. H. LEVY, F.R.C.S.

Kenneth E., aged 16½, was admitted to hospital 9.10.30, with the history of a sudden onset of pain and proptosis in the right eye, six or seven weeks before; this was accompanied by loss of vision.

His vision had been normal previously, and twelve months before he had passed the entrance test for the Merchant Service.

On admission.—Movements of right eye full. Eye was proptosed and not injected. Tension normal. Right vision = perception of movement in a very small nasal field. The eye was hypermetropic

$$\frac{+6{\cdot}0}{+5{\cdot}0}$$

and the disc was pale and raised about 1·50 dioptres.

No signs of general or of nervous disease. Wassermann reaction negative, even after a provocative dose of 606.

10.11.30—Patient remained in hospital for a month. The proptosis and resistance to pressure definitely decreased.[1] The field of vision increased on the nasal side and he was able to count fingers in this area.

On return to hospital 10.12.30, the right field was slightly smaller and the disc markedly pale. The degree of proptosis remains about the same.

The question is what has produced this proptosis and swelling of the disc. It has been suggested to me that there is hæmorrhage into the sheath of the nerve.

Mr. M. S. MAYOU said he had seen this boy on several occasions. The proptosis was now less in extent than formerly. He thought it was due to hæmorrhage. He had seen one or two similar cases operated upon, and a cyst containing cholesterin crystals had been found in the orbit. He thought that some of these hæmorrhages arose from a nævoid condition in the orbit.

Ophthalmoplegia. Case for diagnosis: ? Cerebral Neoplasm, ? Disseminated Sclerosis of Rare Type.—J. F. CUNNINGHAM, F.R.C.S.

Gladys A., aged 37. First seen at Central London Ophthalmic Hospital, 8.12.30, complaining of diplopia of six years' duration.

[1] Confirmed by readings with exophthalmometer.

History (elicited from London Hospital).—Admitted in May, 1930, under care of Dr. Riddoch, with history of pain over right eye and projectile vomiting for years; diplopia, dating from July, 1926. Right pupil then larger than left, with sluggish reaction to light. Paralysis of external rectus, with nystagmus to each side; diplopia on looking to right; optic discs pale. Right-sided facial weakness; bilateral middle-ear deafness. Left Babinski reaction.

Skiagram of skull negative; Wassermann reaction negative; cerebrospinal fluid clear. Was nine months pregnant; labour induced; child died after five days.

Present condition.—Weak action of external rectus. Poor movements up and down. Diplopia in all directions.

$$\text{RV} = \tfrac{6}{18}. \quad \text{With} \begin{matrix} + \ 1{\cdot}0 \text{ D sph.} \\ - \ 2{\cdot}0 \text{ D cyl. ax.}180^\circ \end{matrix} = \tfrac{6}{9}.$$

$$\text{LV} = \tfrac{6}{12}. \quad \text{With} + 2{\cdot}0 \text{ D cyl. ax.}120^\circ = \tfrac{6}{9}.$$

Fundi normal. Right pupil inactive; left pupil reacts to light and accommodation. Left extensor response, knee- and ankle-jerks brisk. (?) Some weakness of right side of palate. No sensory loss.

I only saw the case two days ago, and this afternoon Dr. Grainger Stewart spent a long time investigating it. A mastoid operation has been performed but, as it was on the left side, it is not of much help in explaining her symptoms. Dr. Grainger Stewart thought the case might be one of cerebral neoplasm, or a rare type of disseminated sclerosis. Dr. Riddoch has kindly supplied many of the details.

Mr. J. H. FISHER said that the original onset of the ophthalmoplegia occurred towards the termination of a pregnancy, which had been associated with violent vomiting. The vomiting of pregnancy was now regarded as a toxæmic condition. Many years ago he had recorded (*Ophthalmic Review*, 1898, xvii) a case in which ophthalmoplegia interna had developed, associated with the vomiting of pregnancy. It followed an article on peripheral neuritis accompanying the vomiting of pregnancy, published by Dr. Turney in the St. Thomas's Hospital Reports. Dr. Grainger Stewart had evidently carefully investigated this patient's central nervous system and had found no evidence of focal or local disease in the brain. Peripheral neuritis would explain the ophthalmoplegia externa, and the case could be attributed to toxæmia of pregnancy and peripheral neuritis. Cytotoxins derived from the syncytium cells of the chorionic villi were the source of the toxæmia.

Bilateral Exophthalmos.—A. H. LEVY, F.R.C.S.

E. S., female, aged 53. Prominence of both eyes first noticed in June, 1930. Degree of prominence varies, but never completely subsides. Marked bilateral exophthalmos, with all the usual signs. Eyes injected and watering. Tension normal. No increase in post-orbital resistance. Right vision $\frac{6}{18}$; left vision $\frac{6}{18}$; with $-\ 0{\cdot}75$D. $\frac{6}{9}$ each.

No signs of Graves' disease. Nasal sinuses clear. No general disease of any kind found at University College Hospital by Professor T. R. Elliott.

The patient underwent subtotal hysterectomy seven years ago, and remained well until last June, when this proptosis suddenly developed, with wide palpebral aperture. She has no other signs of hyperthyroidism. A diagnosis suggested is angio-neurotic œdema. From the point of view of the eye, however, the condition closely simulates ordinary Graves' disease: there is proptosis, and there are the Stellwag and von Graefe symptoms, but there is no tremor, tachycardia, or swelling in the neck. The possibility of a chronic thrombosis of the cavernous sinus has to be borne in mind.

Discussion.—Mr. M. S. MAYOU said he thought one feature of angio-neurotic œdema was that the œdema occurred and then subsided, whereas in this case the proptosis had been permanent. [Mr. LEVY: More or less permanent, but sometimes the lids occupy the

normal position.] He (Mr. Mayou) had seen one case of angio-neurotic œdema in the orbit (unilateral) in a girl who had had six attacks, and with each of them she had some proptosis, and became so blind that the pupil did not react. Papillœdema was present. Vision, however, began to recover in forty-eight hours, leaving a central scotoma, which finally cleared.

Miss D. ADAMS said she had heard from University College Hospital that the condition was there considered not to be angio-neurotic œdema.

Mr. LEVY said that the patient had at one time hæmorrhage from the conjunctiva, and that would be one explanation of the old-time reference to "tears of blood."

Retinal Changes after Electric Burn.—A. H. LEVY, F.R.C.S.

This was a patient of Dr. Bainbridge, of Hull, who sent him to me because a question had arisen in regard to insurance, i.e., as to whether the fundus changes and blindness were due to the accident. The doctor had said they were not, but I do not think it safe to assume that they were entirely independent occurrences. Three years ago the man had an accident in which an alternating current of 440 volts passed through his body. He was unconscious, and his life was saved by his leg catching in a crane; he was working high in the air. He was burned about the legs and arm, and was treated in hospital. Six months after the accident the vision began to fail, and had steadily become worse. I saw him in July, 1930. The fundus is extraordinary; there are angeoid streaks and optic atrophy, also choroidal disturbance. I think that the present eye condition is more likely to be the result of the accident than to have occurred independently. There is nothing else to explain it; the patient is otherwise healthy.

Discussion.—Mr. J. H. FISHER said the view he took of the case was, that seeing the fields revealed altitudinal hemianopia one could not judge of the condition by what could be seen with the ophthalmoscope alone. He thought that a man who had received an electric current of such high voltage that it rendered him unconscious for some time, would have a contusion or concussion of the brain. Now he had the upper half of the field in each eye intact, showing that below the calcarine fissure there had been no damage to the centres, but that above that fissure there had been destructive damage to the half-vision centres, both right and left. He had reported (Ophthalmological Society's *Transactions*) a case of bullet wound in which there were definite altitudinal fields, and the lesion caused by the bullet was in the confirmatory position. This present patient, he considered, had sustained damage to the cerebral cortex in both half-vision centres, and this must be taken into consideration, as well as the changes in optic nerve and retina which could be seen.

Mr. LINDSAY REA said he had a patient who had been struck by lightning. In one eye she had a perfect retinitis circinata and complete macular blindness, though there was no perceptible change in the macula. She dated the change from the lightning episode, and the condition had since remained the same. This present patient, having had 440 volts through his body, might have a change produced deeper than those in the retina, and the optic nerves might be involved as well.

Iridocyclitis in Left Eye, with a shrunken globe on the Right Side containing a Sarcoma of the Choroid.—M. S. MAYOU, F.R.C.S.

Patient, male, aged 63.

History.—First seen at Central London Ophthalmic Hospital, 5.12.30, complaining of misty vision in left eye. Two years previously the right eye had been inflamed and painful. It had been treated, without operation, at the Royal London Ophthalmic Hospital.

Present condition.—Left eye: iridocyclitis, keratitis punctata ++. Dense vitreous haze. Pupil dilates poorly. Tension normal. Vision $\frac{6}{18}$, partly. Right eye: shrunken, with no visible cornea, as though sloughing of the cornea had occurred some time previously.

Note from Royal London Ophthalmic Hospital.—In February, 1929, the right eye was in a state of absolute glaucoma, with all the signs of iridocyclitis and secondary glaucoma.

No operation was performed.

POSTSCRIPT.—The shrunken globe was removed under an anæsthetic. It was found to contain a melanotic sarcoma of the choroid of the large round-cell type beginning at the posterior pole. There was no sign of degeneration in the growth. The eye contained no lens and the whole of the cornea had disappeared. In the anterior part of the choroid there were one or two nodules of lymphocytes.

Complicated Cataract of Obscure Origin.—J. H. DOGGART, F.R.C.S.

Patient, female, aged 17, came to hospital in June, 1930, with a history of failure of vision in both eyes. She had posterior cataract in each eye, more advanced in right than in left. The best vision obtainable was, right $\frac{6}{24}$; left $\frac{6}{9}$. Nothing wrong in general health was found, except septic spots on each tonsil; she had had an attack of tonsillitis three months previously. Teeth very good. The tonsils were removed, July, 1930, and there has not, so far, been any further deterioration in sight. There is a typical complicated cataract in each eye, the opacity being mainly in the posterior cortex, deeper axially than peripherally. There are many small vacuoles just under the anterior capsule. No other intra-ocular disease has been found.

[I am indebted to Sir John Parsons for permission to show this case.]

Old Mustard-Gas Burns.—J. H. DOGGART, F.R.C.S.

This man was burned with mustard-gas in both eyes in 1918. He now has a peripheral opacity, porcelain-like in appearance, in the lower half of each cornea, and there are many superficial crystals central to the opacities. The conjunctival vessels, especially of the right eye, show numerous constrictions and dilatations. According to Mr. Foster Moore, who saw many mustard-gas burns during the Great War, this "beading" of the conjunctival vessels is a characteristic sign.

[I am indebted to Mr. W. S. Duke-Elder for permission to show this case.]

? Staphyloma Posticum Verum (Posterior Polar Ectasia).—FRANK W. LAW, F.R.C.S.

A. B., a girl aged 8, brought to me because she blinked excessively. No history of defective vision. I found the left eye emmetropic and otherwise normal. The central refraction of the right eye was − 9D, whereas the inner and outer peripheral parts were approximately emmetropic.

Right Eye.—On examination a fairly normal-looking optic disc is seen, having normal or possibly slightly attenuated vessels; the disc is situated at the bottom of a localized hole at the posterior pole, in depth 9D. The macula—which is the site of pigmentary disturbance—is situated on the edge of the crater; there is pigmentary disturbance around the crater elsewhere, with some choroidal atrophy and sclerotic exposure. It is important to notice that the rest of the fundus is not myopic in appearance, or by refraction. There is a good macular fixation; vision is much reduced, and its exact value I cannot determine.

Cases such as these were first recorded by von Graefe [1] in 1854. Little notice was taken until Weiss [2] in 1876, and Masselon [3] in 1891, redirected attention to them. Otto [4] in 1897 wrote a long paper on these and similar conditions, and claimed to have found 55 cases in 355 myopic eyes, which seems to me a very high proportion. His paper is illustrated by excellent drawings. Schnabel [5] in 1895 also wrote on the condition; he considers it to be always a congenital malformation.

The points of special interest in this case are that (1) the crater is much more regular than usual; (2) the eye is not a myopic eye, but the central fundus refraction is myopic only *post hoc*; (3) the usual concentric shadows are absent.

REFERENCES.

[1] *Archiv. f. Ophth.*, 1854, i, 2. 2] *Ibid.*, 1876, xxii, 3. [3] Ophthalmoscopic Clinique, Paris, 1891 (not traced). [4] *Archiv f. Ophth.*, 1897, xliii, 3. [5] *Zeitschr. f. Heilkunde*, 1895, xvi, 1.

Epithelial Cyst of Iris.—FRANK W. LAW, F.R.C.S.

E. H., a girl aged 19, a picture-frame jointer by trade, gives a history of having had a foreign body in the right eye six months ago while using a steel instrument on 3-ply wood. It was removed by a fellow-worker, and no trouble followed. A week later, quite independently of the accident, she consulted her doctor about the need for glasses; these were obtained from an optician and have been worn since. Three months ago she noticed that the right pupil was not circular; she attended the Royal London Ophthalmic Hospital, Moorfields, December 6, 1930, under Sir John Parsons, to whom I am indebted for permission to show the case.

The left eye is apparently normal, with $\frac{6}{5}$ vision. Right vision is $\frac{6}{6}$ partly, with glasses $\frac{6}{5}$. The right eye is white and quiet; tension normal, pupil reniform in shape, and active. In the anterior chamber, upwards and inwards, is a cyst which, though lobulated, shows no sign, by slit lamp microscopy, of being multilocular, it extends from the angle of the anterior chamber just beyond the pupil margin. The iris stroma behind the cyst is atrophied, and the pigment layer is exposed. The lower lobule of the cyst appears to be divided by an opaque white septum, below which the contents, which elsewhere are only very slightly turbid, are much more nearly opaque, and contain isolated white bodies. Since this septum responds (very slowly, about 30° in 10 minutes) to a change of posture, it must merely represent the upper surface of a fluid of greater specific gravity, occupying the lower part of the cyst. There is no visible corneal scar, and the assumption is that a limbal wound caused the implantation cyst.

The contents of the cyst label it as belonging to the commonest type of implantation cyst, as described by Parsons in his "Pathology of the Eye."

A common position for such a cyst is intra-stromal, the anterior layers of the iris being flattened against the cornea and too atrophic to be seen clearly.

No treatment is proposed unless untoward symptoms, such as raised tension or serious affection of the visual acuity, arise.

Bilateral Corectopia.—FRANK W. LAW, F.R.C.S.

J. C., a boy, aged 13, came to me as a refraction case. He shows extreme eccentricity of the pupils, which are situated upwards and inwards. They are active, and there is no marked dyscoria, such as often accompanies the condition.

One of the most interesting features of the case is the axis of astigmatism, which is downwards and outwards in each eye. There must be a relation between this and the position of the pupils. There is no other visible abnormality of either eye; the corrected visual acuity is $\frac{6}{5}$ right and left, and there are no subjective symptoms.

The normal position of the pupils is, of course, slightly downwards and inwards; Parsons [1] quotes Kotelenan as stating that Patagonians normally have pupils situated upwards and inwards, as in this case. Best [2] in 1894, in a very inclusive paper, describes four types of corectopia:

(1) Without other anomaly, described as rare. This is the type to which this case belongs; (2) With evidence of past inflammation; (3) With ectopia of the lens, normally displaced in the opposite direction to the pupil. This he calls the commonest type; (4) With other anomalies.

So far as I can see, all the proffered explanations are conjectural; that of v. Hippel [3] (localized fœtal inflammation) makes the symmetry of a case such as this very difficult to explain.

REFERENCES.

[1] "Pathology of the Eye," 6th ed. 1930; [2] *Archiv f. Ophth.*, 1894, xl, 4; [3] *Ibid.*, 1900, li, 1.

An Extensive Perforating Injury with Glass.—EUGENE WOLFF, F.R.C.S.

E. H., aged 16, admitted to Royal Northern Hospital, November 3, 1928, having sustained one of the number of ocular injuries usually occurring about "Guy Fawkes' Day." A cracker inside a bottle had exploded and burst the bottle. Presumably a piece of glass hit the patient's right eye. There was a large perforating wound about 1 cm. long beginning in the cornea and passing downwards and outwards through the sclera.

The wound gaped slightly and iris and ciliary body were lying in it, while posteriorly vitreous was exposed.

That same evening under retro-ocular novocain the prolapsed uveal tissue was abscised and a flap of conjunctiva previously prepared was brought over the wound (and over the bared area of sclera). The prognosis given was very bad but the eye settled down rapidly and the boy was out of hospital within 14 days.

His vision now is $\frac{6}{12}$ partly, unaided; and with a cylinder − 3, he gets $\frac{6}{9}$ fully.

The scar of the original injury is just visible and there is some peripheral lenticular opacity. It is I think generally agreed that injuries caused by glass warrant a better prognosis than others. If the cut had been made with anything else the patient would almost certainly have lost his eye.

Discussion.—The PRESIDENT said that there was on record the case of a man who had masses of glass in the vitreous, as a result of a chemical explosion at University College. One eye was almost filled with particles of glass, yet he preserved useful vision in it. The other eye had been lost owing to the injury.

Mr. LINDSAY REA said he had had a case in which flying glass had split the cornea, and also incised an area of the sclera equal to the diameter of the cornea. Part of the iris and ciliary body protruded. He (the speaker) prepared a portion of conjunctiva an inch long, and, cutting away the protruding iris and ciliary body, he slipped the ribbon across and the whole wound healed. He then pared off what was redundant. The vision was not very good, but there was a sound eye after the operation. There was a linear scar across the cornea, and the scar could be seen extending behind the regions of ciliary body in the sclera.

A Pedicle Flap from the Upper Lid to Repair a Gap in the Lower.—EUGENE WOLFF, F.R.C.S.

Patient, male, aged 25.

Bicycle accident six years ago, causing injury to left eyelid and fracture of left maxilla. Came to Royal Northern Hospital for repair of a gap involving inner third of left lower lid.

The conjunctiva was exposed on the surface and formed a pocket which was continually collecting dirt.

Three weeks ago, under general anæsthesia, an incision was made at the junction of the skin and conjunctiva at the margins of the gap. The edges of the wound were dissected up and freed from the maxilla, to which they were adherent by dense fibrous tissue.

Although there was some scarring of the upper lid, I was able to make a skin flap (with its pedicle to the outer side) and stitch it into the lips of the incision without tension. The flap has taken very well, although for a day or two it gave rise to a little doubt. The part of the pedicle which bridges the palpebral fissure has rolled up in the same way that the larger pedicle grafts do. It will be divided and trimmed up in a few days.

[*The report of other cases shown at this Meeting will be published in the next issue of the* PROCEEDINGS *of the Section.*]

Section of Surgery.

[*December* 3, 1930.]

DISCUSSION ON SURGERY IN DIABETES.

Professor George E. Gask : In opening this discussion, it may be useful to state briefly what was our surgical procedure in pre-insulin days ; and with that purpose I have taken a passage from Treves' "System of Surgery" (1898 edition), which gives, I think, a statement of the teaching of that date which was not greatly altered until the introduction of insulin. He says :—

"Diabetes offers a serious bar to any kind of operation with injuries involving open wounds ; hæmorrhage, or damage to blood-vessels is exceedingly grave in the subjects of this disease. A wound in a diabetic patient will probably not heal well. The tissues appear to offer a most favourable medium for putrefactive and pyogenic bacteria."

To enlarge upon that, it was the practice at my hospital, if a patient came in who was discovered to have diabetes, to avoid any form of operation whatever. Further, the reason why every patient had to be examined very carefully, and the urine tested, before operation, was largely in order to find out whether he had diabetes, and if sugar was discovered in his urine the house surgeon crossed him off the operation list.

By the introduction of insulin our ideas have been modified profoundly. Operations previously undreamed of in diabetic subjects have been made comparatively safe. Banting's discovery has had an influence on surgery all over the world. I hope that Dr. Banting will accept the Honorary Fellowship of the Royal College of Surgeons as a recognition of our indebtedness to him.

What should be done in the following instances: (1) In the event of the discovery of glycosuria in a patient for whom an operation of convenience is proposed, e.g., the cure of a hernia, or removal of an appendix in the quiescent period? Personally I would say that, given proper treatment—a proper quantity of insulin—there is no bar to the operation, which may be performed with little additional risk. (2) In the event of the discovery of glycosuria in a patient requiring a life-saving operation, e.g. on account of intestinal obstruction, or of acute appendicitis ? I think that the life-saving operation should not be postponed. The patient should receive a proper amount of insulin, and a course of anti-diabetic treatment after the operation. (3) In a case of gangrene of a limb associated with diabetes ? By that I mean the type of patient with whom we are familiar, one suffering from arterio-sclerosis who has diabetes also, and commencing gangrene of a toe. On this I speak less dogmatically. In the pre-insulin days I think I should have said that such a patient should have that limb amputated as soon as possible, and as high as possible. By "high" I mean that if there was gangrene affecting the toes, the limb should be amputated at the knee-joint, where the collateral circulation is at its best. Since the introduction of insulin that attitude has changed somewhat, and more conservative treatment may now be carried out with safety to the patient. By this I

mean that the limb of a patient with gangrene can be preserved for a time by a proper use of insulin, and that, associated with warmth and light, this will prevent the spread of the gangrene and prevent a dry becoming a wet gangrene. (4) A case of pyogenic infection associated with diabetes, e.g., carbuncle? In this condition more than in any other, insulin treatment should be carried out early and steps to lessen the pyogenic infection should be instituted at once. Suppuration has a serious effect on the diabetic process, and the sooner the infection can be checked, the better for the patient.

My last point is that the anæsthetic of choice is a local anæsthetic, which, with the improved methods lately introduced, can be used in the large majority of cases. I also hold strongly, however, that if local anæsthesia is not available or, for some reason, is not effective, there should be no hesitation in giving a general anæsthetic. Operation must be done quickly and efficiently, and the anæsthetic must be subservient to it. If a gas-and-oxygen mixture is not sufficient, it must be aided by ether, or even by chloroform.

Dr. George Graham: Professor Gask has outlined the treatment which was in vogue before the discovery of insulin. It is interesting to consider how this practice grew up.

In his book on operative surgery, published in 1891, Treves said: "Diabetes offers almost a positive bar to any kind of operation." In 1892, Mr. W. G. Spencer published a paper in the *Transactions of the Medico-Chirurgical Society*, which was followed in 1893 by a paper by Sir Rickman Godlee, and a discussion in the *Proceedings*. These papers showed a complete change of opinion. Mr. Spencer saw two cases, both of diabetes, in which acute sepsis of one limb had developed. The first patient refused amputation and died in diabetic coma; the second also refused operation, and permission for the arm to be removed was not given until he was semi-conscious. He recovered, but continued to pass sugar in his urine. Mr. Spencer pointed out that the amount of sugar excreted by a chronic diabetic was greatly increased by inflammatory affections. Later in the paper Mr. Spencer said that diabetic gangrene could be operated upon by following the rules already established for other gangrene. It was as a result of Mr. Spencer's paper that Sir Frederick Treves modified the statement in his book.

Insulin has entirely altered the outlook, and it is now possible to perform any operation if the other conditions are suitable.

With regard to Professor Gask's first category, it is necessary to be sure of the diagnosis, for not everyone who has dextrose in the urine has diabetes; it may be that he has either renal glycosuria, or the so-called "lag curve," and the diagnosis can only be made by a proper sugar-tolerance test. Whenever time permits this should be done, because if the patient has not diabetes, no special precautions are necessary. If the patient has diabetes, and there is time, he should be prepared for operation by means of dieting and insulin. It is usually possible to do this in from four to seven days, unless the disease is severe. I think that every large hospital should now have an expert dietetician, and a special kitchen, to ensure that the diabetic patient has the diet he is ordered. Before the operation he should always have 50 gr. of sugar, and from 15 to 20 units of insulin should be given thirty minutes before the sugar. This sugar is given to ensure that there is plenty of sugar in the body, and as much glycogen in the liver as possible, in case it is necessary to use ether as a general anæsthetic.

For the acute case—appendicitis or the acute abdomen—when an immediate operation is necessary, an estimate of the blood-sugar should be made, if possible, so as to make certain of the diagnosis. If the patient has diabetes, 50 grm. of dextrose should be given, because some patients with severe diabetes do not have a high blood-sugar. If a large dose of insulin is given, and the patient has not a

high blood-sugar, much harm might result. If the patient is very ill, 50 or 75 units of insulin should be given, but if the condition is mild, 25 units may suffice. If there is vomiting, sugar must be given intravenously, in a pint of saline. The saline is also beneficial, as it replaces some of the salt which has been lost by the vomiting.

After-treatment.—The dietetic treatment which is suitable to a patient not suffering from diabetes should be given to the diabetic patient, and if the urine can be collected and the blood-sugar examined, the appropriate dose of insulin can be guessed. The estimation of the blood-sugar is of great help in gauging the right dose of insulin, but it is often necessary to do this on the result of the urine examination.

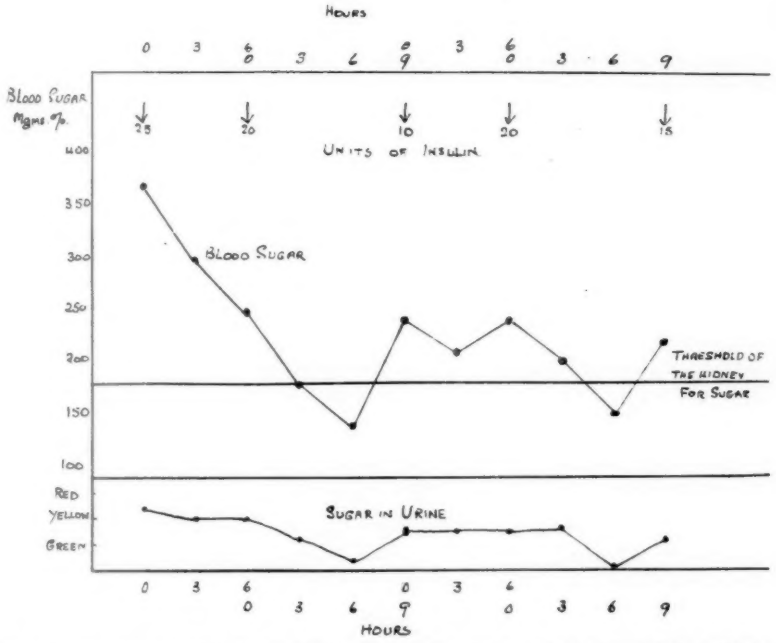


FIG. 1.—Showing a method by which the dose of insulin can be gauged by means of Benedict's qualitative test for sugar in the urine.

The urine should be collected every three hours approximately. The insulin is given or withheld according to whether sugar is present or absent from the urine in the specimen four or six hours after the insulin. The dose of insulin is increased or decreased according to the amount of sugar in the urine.

The course of the blood-sugar in comparison with the urine tests explains the reason for the increase or decrease in the insulin.

The nurses should know the signs of hypoglycæmia, and should be prepared to give either sugar by the mouth, or ten units of pituitrin (1 c.c.) subcutaneously.

I am in agreement with the view expressed by Spencer in 1892, and confirmed by Cuthbert Wallace in 1899, that "sclerosis of the arteries is always present in so-called

diabetic gangrene." The diabetes does not cause the gangrene, and is itself made much worse by the gangrene. It is possible that a badly chosen diet with excess of fat may help to cause the sclerosis of the arteries. I think, therefore, that the name "diabetic gangrene" should be abandoned, as it gives a wrong impression of the pathology of the condition.

As soon as a pyogenic infection is diagnosed it should be dealt with, as all such conditions adversely affect the sugar-tolerance. The longer the infection persists, the worse the diabetic condition becomes.

I have recently seen two cases of carcinoma of the breast in which radium had been used. A patient, aged 77, who had had diabetes for many years. She refused insulin, and had lately become weaker. She had a small growth in the outer quadrant of one breast, and Sir Charles Gordon-Watson decided to insert radium needles. The diabetes was mild, and she was given a diet containing 100 grm. of carbohydrate. In a week's time, the urine was sugar-free, and the blood-sugar normal, on a dosage of 25 + 24 units of insulin. Six days after the insertion of 33·8 mgm. of radium element, the insulin had been increased to 44 + 52 units, and this just kept the urine sugar-free. Thus the radium had caused an increased demand for 47 units. Seven days later, the insulin requirements had decreased to 48 units. In another patient, the insulin requirements rose from 18 to 28 units after 60 mgm. of radium element, and decreased again to the original figure in a week's time.

I feel sure that if surgeons tested the urine passed after the evening meal each day, during the period of the radium treatment, they would find that some of their elderly patients passed sugar. If so, the general condition during the week of treatment would be improved by the injection of small doses of insulin. It is probable that this condition also occurs in the course of severe pyogenic infections in elderly patients, and the giving of insulin to such a patient would reduce the amount of sugar in the blood and all tissue fluids, and so render the conditions for the growth of bacteria less favourable, and in doubtful cases might greatly increase the patient's chance of recovery.

Dr. R. D. Lawrence said that for practical purposes he would draw a distinction between ordinary surgical procedures in diabetics, and surgery in conditions produced (entirely or partially) by diabetes. In the first group he felt that the surgeon need have no special considerations or responsibilities. But the second group required special consideration. He thought it might interest Members to see statistics of a series of 163 cases, which gave thirteen deaths.

	No.	Deaths	No insulin
Cataract	44	0	26
Carbuncle	14	1	1
Gangrene	27	—	2
Thigh amputation 15	—	4	0
Other Operations ...	78	8	15
Totals ...	163	13	44

Cause of Death.

Coma	1	Heart failure ...	3
Pneumonia ..	5	Uræmia ...	1
Embolus... ..	2	Septicæmia ...	1

The surgeon, unless he were looking after the medical part of the treatment, need not consider diabetes if it could be properly controlled; to do so often involved much work and time, and required a good deal of experience. The chief danger in operations in these cases was acidosis. Dr. Graham had shown that a glycosuria lasting only a few days was of little consideration so long as the sugar was controlled,

so that the patient was not distressed by great thirst. He was accustomed to give 100 grm. of carbohydrate beforehand, and he tried to continue the same diet afterwards, modifying the insulin given according to the blood-sugar test. No standard was applicable to every case, and operation affected people differently. In some the insulin needed to be trebled after the operation, while other patients required only a slight addition. Also there were often conditions of changing sepsis, and as the sepsis became less the diabetic condition improved.

As to the question of the best anæsthetic for diabetic cases—he was sure chloroform was the worst, primarily because it had the greatest toxic action on the liver—and the diabetic liver had never, under the best conditions of treatment even, as much glycogen as the normal liver. So long as no local sepsis was present, he agreed with Professor Gask that the anæsthetic of choice for these cases was a local one. For lower limb conditions spinal anæsthesia was ideal. He had tried avertin anæsthesia in two cases, and had been well satisfied with it. In some of the large diabetic clinics in America avertin had been used almost exclusively for two years. Gas and oxygen with the minimum of ether was usually satisfactory. It was a drawback for the diabetic to vomit after the operation, and if he did not have carbohydrate and insulin he drifted into acidosis, and the vomiting became worse. The anæsthetic of choice was one which caused no vomiting or less than usual.

With regard to post-operative treatment, he would relate two cases showing that the condition must be closely watched from hour to hour, almost; or at least from day to day.

(I) This was a case in which hysterectomy was to be performed in a woman aged 50, who had had diabetes for two years. He (the speaker) had been asked if he could prepare her for operation in two or three days. When admitted, she was having 14 units of insulin daily and a diet containing 70 grm. of carbohydrate. The blood-sugar was 0·25. On the day before operation she had 34 units of insulin and a little more carbohydrate, and there was normal blood-sugar. After the operation she could not take the evening carbohydrate, which was Benger's food, and glucose had to be given rectally. Often Benger's food, grapes and milk were tolerated by patients whom glucose made sick. On the day after operation there was sugar in the urine and a good deal of acetone. Sixty units of insulin were given, in three 20-unit doses, and the carbohydrate was increased a little. The patient needed added insulin for three days, after which a gradual improvement enabled a resumption of her previous treatment, and twenty-one days after operation she was on less insulin than before the operation.

(II) This was an emergency case of gangrenous gall-bladder in an old and obese woman, in whom diabetes was not discovered until half an hour before the operation. A good deal of sugar and acetone were found in the urine; the blood-sugar content was not known. Ten units of insulin were given, and operation was carried out. Next morning the patient was in a state of collapse, and had slight air-hunger; obviously diabetic coma was developing. The blood-sugar was 0·546, and he (the speaker) gave her 100 units of insulin. No urine could be obtained for the rest of that day. A few hours later the blood-sugar was found to be dropping, and she had 15 units of insulin four-hourly and 20 grm. of sugar. Next morning some urine was obtained, and it contained no sugar and no acetone. For one more day the treatment was continued; then she had less carbohydrate, the insulin was reduced to 40 units a day, and she made good progress; the gall-bladder sloughed. On the fiftieth day after operation she was on a diet without insulin. Recently, two years later, she was well and was not having insulin. In emergency cases four-hourly doses of insulin should be given, and corresponding glucose.

When carbuncles existed, the surgery should be performed at once. With regard to gangrene, septic feet were frequently found in association with diabetes. Gangrene occurred in diabetics only when they also had arteriosclerosis or other severe

arterial degeneration. When the pulsation in the dorsalis pedis artery was good, gangrene did not occur; hence, given a good circulation, the case could be treated on general surgical principles. When the dorsalis pedis did not show good circulation, X-rays might reveal calcification in the vessels throughout the limb; there might be obliterative endarteritis, or a combination of that with the previously-mentioned condition. X-rays, however, might mislead the observer. Because calcification was apparent that did not necessarily mean that there must be a high amputation. He divided these cases into three groups. When dry gangrene was present there was no need for hurry; one should treat the diabetes by dieting, then wait and see. The best result was a mummification and a separation of the gangrene. The other extreme was a rapidly-spreading sepsis and lymphangitis. In such a case the limb could not be saved; one could only save life. There should be a high amputation, at the same time controlling the diabetes. The difficult cases were those intermediate between those two. Practically all cases of gangrene which he saw were complicated by sepsis. He was becoming more conservative in his advice on these cases. If, in a day or two, the sepsis and œdema were diminishing, he counselled waiting, longer and treating on conservative lines.

So far in this discussion the diabetic acute abdomen had not been mentioned; it was difficult to make up one's mind how best to treat such a condition. The ordinary acute abdomen was simulated by the ketosis alone. The patient might be admitted complaining of intense colicky pain, and there would be found tenderness and some rigidity. In such cases it was almost impossible to know whether one was dealing with an appendix, a perforated viscus, or an acute diabetic abdomen. A raised temperature was in favour of the symptoms not being entirely due to the diabetic condition. Leucocytosis was no help, because in diabetic coma and severe ketosis there was nearly always a leucocytosis of over 20,000. If there was a strong suspicion of the presence of an acute disease, such as appendicitis, urgently requiring operation, it was best to operate at once, even though one was proved wrong.

Mr. Cyril A. R. Nitch said that when the surgeon was unable to obtain the constant advice and assistance of the physician and the biochemist, there were certain points in connection with the use of insulin which he should realize. The most important of these were: (1) When there was no urgency and when a patient could be stabilized by diet alone, only a small dose of insulin would be required before, and possibly after, an operation. (2) When the usual food intake was diminished by vomiting, or after gastro-enterostomy or tonsillectomy, the dose of insulin must be reduced or omitted, provided the urine was sugar-free. (3) Pituitrin and epinephrin sometimes neutralized the effect of insulin. (4) In emaciation and sepsis the effect of insulin was sometimes so pronounced that even a small dose might cause hypoglycæmia. (5) Hypoglycæmia might set in if the dose of insulin was not reduced during recovery from an operation, or from sepsis, or after removal of a large area of sepsis, such as a gangrenous leg. The nurse in charge should be warned of the possibility of hypoglycæmia, especially after any operation in which feeding or dieting was difficult, and should be told to notify the surgeon immediately of any unusual symptoms, such as increased pulse-rate, restlessness, delirium, or mania. In such a case the blood-sugar must be estimated as soon as possible, and in the meantime glucose should be given by mouth. (6) As frequent blood-sugar examinations after an operation might be very trying to the patient, or difficult to carry out, the surgeon would find the application of Benedict's test, as advocated by McKittrick and Root, a reliable guide to the appropriate dose of insulin at any given time. The urine was tested by Benedict's method, two-, three-, or four-hourly, after the operation, according to the severity of the pre-operative diabetes.

If it turned orange 15 units of insulin should be given.
" yellow 10 " " " "
" green 5 " " " "
" blue 0 " " " "

When the patient was sugar-free 100 c.c. of orange juice should be given to prevent hypoglycæmia. In cases of urinary obstruction an in-dwelling catheter was advisable for this test, otherwise a urine which had really become sugar-free might give a positive Benedict reaction from contamination by sugar-containing residual urine. He (Mr. Nitch) agreed that there was little (if any) unusual danger in an operation of convenience on a diabetic who had been properly balanced by diet and insulin. [Mr. Nitch then described the pre- and post-operative treatment of elective and emergency cases employed at St. Thomas's Hospital.]

For coma and pre-coma no routine or rule was possible. The physician must individualize and gauge the size and number of doses of insulin and carbohydrate by the percentage of sugar in the blood and urine, and by its effect on the breathing and the general condition of the patient. It was of the utmost importance to administer plenty of fluid by some means, as these patients were dehydrated rapidly by the deep breathing.

Anæsthesia.—For operations below the umbilicus, spinal or local analgesia was best. Gas-and-oxygen was only suitable for abdominal operations and operations of long duration, when given by an expert. The disadvantages of ether were several, especially its proneness to cause sudden acidosis. The dangers could be minimized by skilful administration and careful after-treatment.

Gangrene.—Two clinical varieties were recognizable: (1) Due primarily to arteriosclerosis, or senile gangrene in a diabetic, and (2) diabetic gangrene, due to infection, aggravated by diabetes, and usually, though not always, complicated by a defective circulation. In the first the diabetes was often mild, the predominant features being extensive arteriosclerosis, little or no evidence of collateral circulation, often severe pain and an area of gangrene, which might be superficial and limited, total and limited, or total and extensive. As there was usually no great urgency in these cases, the diabetes should be investigated and stabilized before active surgical measures were adopted. These would vary with the type of gangrene, the degree of pain, the condition of the patient, and their combined effect on the diabetes.

Non-operative measures were applicable to superficial gangrenous patches or ulcers, and to gangrene limited to the whole or part of a toe when the dorsalis pedis artery was not completely occluded, or, if it was occluded, when there was evidence of a collateral circulation, when pain was not severe, and when the diabetes was not being aggravated by the gangrene. In these cases the surgical treatment consisted in careful warmth, local applications to prevent sepsis, Buerger's exercises to stimulate the collateral circulation, and any means, such as artificial sunlight, to improve the general condition of the patient.

Operative measures were required: (1) When it was thought that the gangrene was stimulating the diabetes; (2) for sepsis; (3) for severe pain; (4) for gangrene of one or more toes and (5) when there was no evidence of a collateral circulation. They consisted of: (1) Incision and drainage for sepsis; (2) amputation of a toe, when the dorsalis pedis was patent, when the foot reacted to Buerger's exercises, and when the pain was not severe; (3) high amputation when sepsis or gangrene was spreading, when the collateral circulation was poor, when pain was severe, and when the diabetes was being aggravated. In some cases preliminary ligature of the femoral vein improved the collateral circulation to such an extent that a successful low amputation was possible a week or ten days later, but if there was the least doubt, the amputation should be above the knee. The second variety, diabetic gangrene,

often occurred in younger patients, with less degenerated arteries, consequently local applications, incisions and drainage, and even minor amputations might be successful, but when local infection was extensive, or when sepsis or gangrene was spreading, high amputation should be performed without delay.

Dr. Otto Leyton said that he did not consider the presence or absence of a pulse of vital importance; at the London Hospital for many years it had been customary to place an oscillometer around the ankle of most of the diabetic patients to record the condition of the artery. Occasionally when there was no recognizable pulsation at the ankle a gangrenous patch on the foot had healed.

All cases of gangrene were treated conservatively. The diabetes was controlled, the concentration of sugar in the blood being kept between 0·15% and 0·08%; the foot was bathed in hot hypertonic saline for periods of half an hour or more and then carefully dried with spirit and kept warm by a small radiator in a cradle. When this treatment proved unsuccessful, amputation had been performed above the knee, when there was no pulse at the ankle, until three years ago, and now the least possible amount of gangrenous tissue was removed. A patient whose one occupation was gardening had pleaded for retaining half his foot, asserting that if the first operation was not a success he would submit to a second quite cheerfully. A Syme operation seemed to be especially unsuitable in a case in which there was any obliterative change in the arteries, because the nutrition of the pad of tissue had to be carried on by the vessels passing through a very small piece of skin. At the operation a tourniquet proved unnecessary; the arteries did not spurt and there was very little oozing of blood. He thanked Mr. Cairns for performing the operation, but felt certain that the time expended was wasted.

The result, however, proved quite successful, and eighteen months later when gangrene developed in the other foot of the patient, and spread in spite of all treatment, including the production of pyrexia, another Syme was performed with the same success. The patient was still able to work in his garden with the assistance of artificial feet.

On discussing the matter with Dr. Brown, of the Mayo Clinic, he (Dr. Leyton) had learnt that at that institution they were in the habit of operating at a site where pulsation was absent in cases of gangrene in thrombo-angitis-obliterans—with 70% successes.

One would not expect so high a percentage of successes in diabetic gangrene, because the change in the collateral circulation would be greater. The fact, however, was established, namely, that a pulse in the artery was not a *sine qua non* for a successful operation. He wished to refer to the administration of insulin by the mouth in the preparation of patients who possessed a rooted objection to hypodermic injections. He had tried a great number of substances which, the manufacturers had assured him, when administered orally, acted as well as insulin hypodermically. His experience had been that all had been more or less useless. Recently, however, he had been able to confirm the observations of H. N. Mukherjee, who stated in a paper published in the *Calcutta Medical Journal*, January, 1930, that the phosphotungstate of crude insulin administered to a rabbit by the mouth led to typical hypoglycæmic symptoms along with a reduction of the concentration of sugar in the blood to 0·04%. In the October number of the same journal he referred briefly to three cases of diabetes mellitus, who appeared to have benefited by taking the phosphotungstate of crude insulin by the mouth. He (the speaker) had used phosphotungstate of pure insulin, prepared by the dispenser of the London Hospital, with very promising results. On inquiry whether the salt was likely to prove poisonous he learnt from the Professor of Pharmacology at the University of Edinburgh that Waltner had found that 2% of tungsten salts could be added to the food of rats for six months without producing any recognizable results.

It was not, however, permissible to conclude from this that the phosphotungstate of insulin would prove innocuous if taken for months or years, but since there was little doubt that for a brief period it did no harm, it might be used with advantage for patients who had to be prepared for operation, and who would need the drug for a few weeks at most.

Dr. P. J. Cammidge referred to the high proportion of diabetic patients with septic feet and sepsis in other parts of the body, who, when carefully treated with insulin by injection and locally, improved and could be tided over without surgery.

One of the first of his (Dr. Cammidge's) cases was operated upon by the late Dr. Williamson. The patient had a large fibroma, and it was considered essential that it should be removed. She was prepared as satisfactorily as possible by dieting, and spinal anæsthesia was used. For three days after the operation she did well, then coma developed and she died. Since then he had always been careful to avoid operation whenever possible, until insulin was introduced. His experience with insulin had been so remarkable that he now had no hesitation in advising operation, and he was inclined to think that patients who were carefully prepared for operation by treatment with insulin seemed to do better than the average patient who did not have insulin.

Another point which needed emphasis was the anæsthetic employed. Recently those of his patients who were operated upon had had avertin as an anæsthetic, and it had proved very satisfactory. Most of them had gas-and-oxygen afterwards and some had a small quantity of ether as well. On the whole, he had obtained better results with avertin and gas-and-oxygen than with any other form of anæsthetic for his diabetic cases. It was his custom to give not only glucose and insulin before the operation, but, if possible, an intravenous injection of glucose immediately after, with a considerable quantity of fluid, before the patient was returned to bed. It had been found that this helped to prevent post-operative vomiting, which was the most serious thing that could happen to a diabetic, for it meant dehydration of the tissues and the loss of important constituents, and prevented the patient from taking the carbohydrate which was essential. After operation he (the speaker) tried to give 80 to 100 grm. of carbohydrate with a corresponding dose of insulin for three or four days.

Another point he wished to mention was the importance of controlling the treatment throughout by blood-sugar analyses. In some cases it was difficult to get a specimen of urine, and a blood-sugar estimation was a much more reliable indication than any urinary analysis. For practical purposes extreme accuracy was not necessary, and a sufficiently reliable blood-sugar estimation could be done quickly and easily. This occupied only a few minutes, and such a test could be made every hour without inconvenience, if necessary.

Mr. J. B. Hunter said that with regard to the ordinary type of cellulitis which occurred in diabetics, in a comparatively young person, who perhaps had never been under control or had been under control but had drifted away from it, and in whom there was severe cellulitis—without obvious fluctuation or presence of pus which appeared to call for urgent treatment—it was not necessary to operate, for under insulin treatment the cellulitis became localized and the evacuation of the abscess enabled the condition to clear up.

He agreed as to the frequency of septic feet in these cases, and said that often these patients began with a sore on the toe, without obvious gangrene, and rather indolent in type. Patients were treated by their local doctor for some time, and then the condition gradually spread on to the dorsum of the foot. At that stage they came into hospital, and were put to bed. He felt sure that this was the wrong

line of treatment ; they should be treated like heart cases, i.e., seated, because the recumbent position facilitated the spread of sepsis to the tendon sheaths, and continued however much was done in the way of sugar control, so that eventually a high amputation had to be performed.

His other point was not surgical. In cases of diabetes, if one was going to operate, it was much better to give the patient full carbohydrate diet and have the sugar controlled by insulin, than to try to control it by diet alone.

Section of Urology.

[*November* 27, 1930.]

Carcinoma beginning in a Sacculus of the Bladder.—SYDNEY G. MACDONALD, F.R.C.S. (President).

This specimen was excised from a man aged 65, who for three years had suffered from urinary obstruction due to a large adenomatous prostate. Two or three days before I saw him he had had hæmaturia. The urine was blood-stained and infected, and there were 15 ounces of residual urine. Cystoscopy showed a large projection of the prostate and the opening of a sacculus on the right side, well clear of the ureter. The sacculus was found—on cystostomy—to contain a growth, therefore both growth and sacculus were excised, but unfortunately there was a rapid spread of growth, which fungated through the suprapubic wound. On microscopical examination, the growth proved to be a round-celled carcinoma.

Discussion.—Mr. H. P. WINSBURY WHITE said he agreed that it was almost impossible, or very difficult, to get rid of infection after excision of a diverticulum, but he wished to relate a case in which a man, aged 61, had a diverticulum practically as large as the bladder itself. He (Mr. White) had excised the sac, and the patient did very well. That was five years ago. The patient still had an infected bladder, but his general condition remained good. Not more than one or two ounces of residual urine remained, and that fact, he thought—considering that the diverticulum had held more than a pint—justified the operation.

The PRESIDENT said that from the point of view of infection, one or two ounces of residual urine was as bad as six or seven ounces. These patients were not always of "prostatic age." He had recently had a case in a man, aged 30, who had a sacculus containing a large stone. Operation had been difficult, and had necessitated transplantation of the ureter; there was no obstruction. There was a developmental deficiency of the bladder musculature in all these sacculus cases, and excising the sacculus diminished, but did not abolish, the residual urine.

Mr. CLIFFORD MORSON said that in all these cases of single large diverticulum the condition was of congenital origin, and in all there was an absence of part of the wall of the bladder.

Mr. JOCELYN SWAN said that four years ago he had operated on a man aged 28, who had had no obstructive lesion.

Mr. FOWLER WARD said that he had had a case in a child aged 18 months. A catheter could be passed comfortably, but as soon as the use of the catheter was discontinued there was retention again. A cystogram showed a diverticulum between the two ureters, and the only thing to do was to try to remove it. This was done, and the child died. There was no evidence of infection.

Unusually Large Papilloma of the Bladder. — DUNCAN C. L. FITZWILLIAMS, C.M.G., F.R.C.S.

T. K., aged 50. Complained of burning sensation on passing water, and three months ago had passed blood on two occasions. Had had frequency for two months.

Cystoscopy, 23.9.30.—Very little fluid could be passed into the bladder. Nothing seen by cystoscope, owing to bleeding. Portion of tissue afterwards passed in urine looked like a piece of tumour, but on microscopic examination was reported to be granulation tissue.

Operation, 7.10.30.—On opening the bladder it was found to be completely filled with a soft tumour. The mass was removed piecemeal. The operation was accompanied by considerable hæmorrhage.

Pathological Report.—"Villous papilloma of the bladder. (Weight 1 lb. 2 oz.; wet 1½ lb.) The connective tissue stroma is more cellular than usual, and is infiltrated with eosinophil leucocytes. There is no histological evidence of malignancy."

Discussion.—The PRESIDENT said that the tumour did not look to him like a benign growth, and he was suspicious of malignancy.

Mr. FOWLER WARD said that he had had a case in which he could not cystoscope. The whole bladder was found to be a mass of granulation tissue; this he had removed, and had then put in a drainage tube. He thought that it must have been a malignant growth, but a few months ago the patient's doctor had written stating that the man had been perfectly healthy with the drainage tube in situ, and there had been no further hæmorrhage.

Carbuncle of Kidney.—A. CLIFFORD MORSON, O.B.E., F.R.C.S.

This carbuncle was removed from the right kidney of a man aged 57, who had suffered from pain in the right loin and fever. The fever had persisted for two months, following an attack of boils. A diagnosis of perinephric abscess was made, but at operation no pus was found beneath the diaphragm, or around the kidney. On exposure of the kidney, a carbuncle was found, invading the whole of the upper pole, and another the size of a threepenny-piece was discovered in the lower pole.

Nephrectomy was performed. The patient survived the operation one month, when he died of chronic septicæmia.

It is doubtful, in these cases, whether the patient's life can be saved by nephrectomy. In fact death may be even accelerated. This condition, fortunately, is very rare, but should a similar case occur in my practice, more conservative measures, such as local excision and drainage, will be adopted.

Previous to operation, no bacteriological examination of the urine was made, but chemical analysis revealed traces of albumin and blood.

Discussion.—Mr. CYRIL NITCH said he agreed that the right treatment of these cases was incision rather than nephrectomy. He had had a similar case in a nurse. It was thought that she had a perinephric abscess, and at operation he had found a similar condition to that in the present case. He incised the kidney and put in a drainage tube, and after a stormy convalescence the patient recovered. It was a secondary infection.

Mr. MORSON (in reply) said that he had not tried mercurochrome in carbuncle of the kidney, but he had used it in other blood infections of the kidney, though without very good results.

Specimen: Ruptured Kidney.—E. W. RICHES, M.S.

Patient, a man, aged 34, was wheeling a two-handled barrow when a lorry knocked one of the handles violently into his right side.

Condition on admission to Middlesex Hospital.—Temperature 97° F., pulse 78, respiration 24. Complaining of severe pain in the right side. Tenderness in right loin, but no swelling. Urine contained blood, intimately mixed.

Progress.—After 24 hours the pulse had not risen above 78, nor the temperature above 99° F. Pain and tenderness persisted, and there was some pain in the left upper quadrant. Hæmaturia had diminished.

After 48 hours the pulse had risen to 90, temperature 100° F. Tenderness had increased in the right loin and had spread to the left side. There was no hæmaturia. Operation was undertaken.

Cystoscopy.—Small clot in right ureter; clear efflux from left.

Operation: Right nephrectomy.—Extravasation of urine and blood-clot in the perinephric tissues, but no active bleeding. The peritoneal cavity contained no urine or blood, but there was a small laceration on the under-surface of the right lobe of the liver.

On the ninth day after operation the patient died suddenly from pulmonary embolism.

On post-mortem examination a large clot was found, filling the pulmonary artery and extending into both right and left branches; its site of origin could not be determined. The right kidney bed showed evidence of old retroperitoneal hæmorrhage, and staining extended up behind the right pleura.

The specimen shows a transverse rupture extending from the cortex to the pelvis; the two halves are separated by a space of about $\frac{3}{4}$ in. which is filled with blood-clot.

Clinically the outstanding feature was the almost complete absence of general, as opposed to local, signs. The question as to whether immediate nephrectomy should have been performed is a point for discussion.

Discussion.—Mr. FOWLER WARD said that he had at present the case of a man with ruptured kidney. He had been thrown off a bicycle and two days after the accident had come to hospital complaining of pain in the right loin. A considerable quantity of blood was passed. The pulse was 90, and there was some distension and rigidity on the right side. The tongue was coated, and the temperature was 100° F., and he (the speaker) had decided to wait. The man was at present better than formerly. In some of these cases of ruptured kidney, if one could hold one's hand from operation there was a fair chance of safety; if there was a large hæmorrhage, one must operate.

Mr. H. P. WINSBURY WHITE said he thought that Mr. Riches had been right in waiting before he operated. When he (the speaker) had been Registrar at the Royal Free Hospital, he had investigated forty-four cases of injured kidney, with regard to treatment, and 73 per cent. of these had recovered completely without operation. Since then he had been treating his own cases of injured kidney in the hope that he would be able to effect a cure without surgical interference.

He had recently dealt with four cases of the kind. The first three were those of two young men and a child who had been struck in the side. There had been hæmaturia for some days, but all had recovered well under treatment. The fourth case was that of a child who had fallen down and injured an already diseased kidney. That was in a different category, and he had been obliged to operate.

At the first sign of sepsis one should operate; that was the stage at which Mr. Riches had intervened in his case.

Mr. H. W. S. WRIGHT said he had had a case in a youth, aged 20, who had been struck in the side by the handle of a barrow, and was admitted to hospital on account of hæmaturia. On examination the right loin was found to be tender, but not swollen. Next morning there was a large tender swelling in the right loin, which was explored on account of the increase in size. At operation the anterior and posterior surfaces of the kidney were split transversely from the lateral margin to the pelvis. The kidney was sutured and the wound drained. The patient made an uneventful recovery, the renal function being good and the pyelogram nearly normal.

Adenoma of the Kidney giving rise to a large Hæmorrhage.—H. W. S. WRIGHT, M.S.

This occurred in a woman aged 70, who, for six months, had a small, painless swelling in the left side of the abdomen. A fortnight before admission she complained of great pain in that side, and the swelling suddenly became much larger. It was so mobile that it was at first taken to be an ovarian cyst. It is not certain whether the tumour is a carcinoma or an adenoma, because, although the cells are regularly arranged and there is a tendency to tubule formation in parts, there is also some infiltration of the capsule. This appearance may, however, be due to recent hæmorrhage.

Mr. JOCELYN SWAN said that recently he had a case in which he had diagnosed hypernephroma. He saw blood coming from the right ureter, and the pyelogram showed a filling defect in the upper pole of the kidney, and that the upper calyx was deformed. The kidney was exposed and a tumour the size of a large marble was found in the upper pole. Nephrectomy was performed. The pathological report on the section was "adenoma; into which hæmorrhage had occurred."

Two Cases of Double Renal Pelvis and Hydronephrosis.—H. P. WINSBURY-WHITE, F.R.C.S.

(I) The first case was in a boy of 8 years, who had complained of pain in the left side.

Cystoscopy showed two ureteric orifices on the left side and one on the right. The intravenous injection of indigo-carmine showed the dye being ejected from the right ureteric orifice and the lower orifice on the left side within six minutes, in good

concentration, while none appeared from the upper left orifice within fifteen minutes. Ureteric catheters were passed into both ureteric orifices on the left side and pyelography was carried out (fig. 1). This showed a double pelvis of the left kidney, with hydronephrosis involving the lower part.

I cut down on the kidney and then found that it was not difficult to palpate the line of demarcation between the dilated and the non-dilated renal tissue. This at once suggested the possibility of resection of the dilated portion, and after separating the blood-supply to the two parts I was able to carry this out. Three

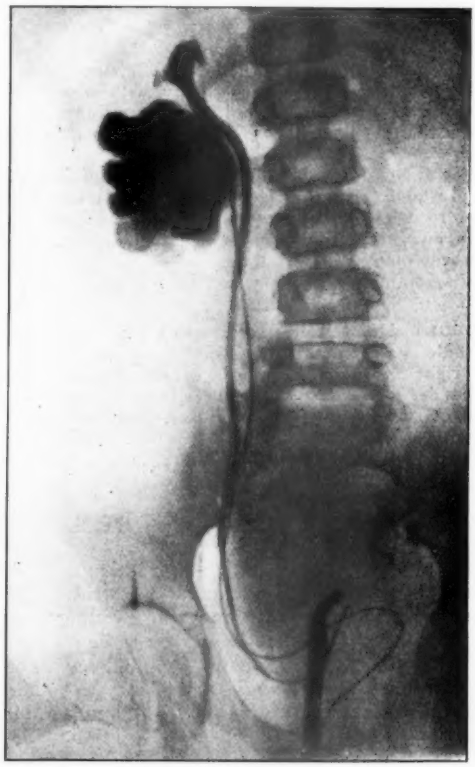


FIG. 1.—Double left kidney.

months after the operation I cystoscoped the child again. On this occasion an intravenous injection of indigo-carmine showed the persisting renal tissue of the left side to be functioning normally. A pyelogram (fig. 2) carried out at the same time indicated the same appearance as was evident in the upper part of the pyelogram when pyelography was carried out on the first occasion.

(II) The second specimen I removed from a married woman, aged 33, who made a good recovery. During her first pregnancy, six years before, she had suffered a good deal of pain in the left side, with pyuria and pyrexia. On the occasion of her first visit to me she was four months advanced in pregnancy.

On examination I was able to make out deep resistance to palpation in the left loin. A plain skiagram was negative to stone, and examination of the urine showed a complete absence of any pathological elements. Cystoscopy showed a healthy bladder, and indigo-carmine, injected intravenously, was seen coming from the right ureteric orifice within five minutes, in good concentration, while none had appeared from the left side within twelve minutes of the time of the injection. Intravenous pyelography was carried out with uroselectan. This showed a deformity of the left renal pelvis, which was distorted by pressure from a rounded mass lying below it, suggestive of a unilocular renal cyst.

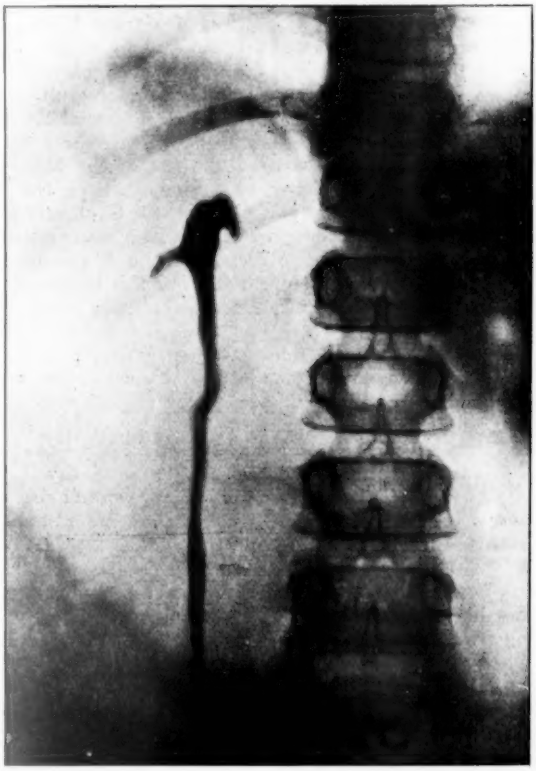


FIG. 2.—Remainder of kidney after resection of hydronephrotic half.

I cut down on the kidney and removed the whole organ, and it was only after hardening and then carefully dissecting the specimen that the true nature of the condition was revealed. The active renal tissue is perched like a triangular cap on the top of the distended sac, which is lobulated and uniformly thin and fibrous. As is inevitable with double pelvis, two ureters are present. These may join at any part of their course to the bladder, or they may not join at all. In this case they are observed uniting on the surface of the dilated portion.

A point of special interest here is that the lower ureter is seen to be compressed by the normal inferior branch of the renal artery, and on looking at the specimen it is quite apparent that this has occurred as a complication of the hydro-

nephrosis, because as the distending pelvis has followed the line of least resistance, it has bulged forward, dragging the ureter with it over the inferior vessel, which now compresses it against the pelvis. There is no doubt that this complication has added considerably to the original cause of the retention. As in many cases of hydronephrosis, in this particular case one cannot be certain what was the actual cause.

The point of common interest in these two specimens is that it was the lower pelvis in each case which was the seat of the dilatation.

Three Cases of Hydronephrosis Associated with Hæmaturia.—H. P. WINSBURY-WHITE, F.R.C.S.

In my first case I am showing a drawing of a fresh kidney laid open within a few hours of its removal. As seen in the drawing there was a widespread inflammatory injection of the mucosa of all of the calyces and the pelvis. Microscopy of the renal tissue showed that the glomeruli and tubules were engorged with blood, and, moreover, the whole of the renal tissue examined was found to be infiltrated with inflammatory cells. Thus there was clear evidence in the naked-eye appearance of the mucous surface of the kidney and on microscopic examination of the renal tissue, that the cause of the bleeding was an inflammatory complication of the hydronephrosis. Cystoscopy had previously shown blood coming from the right ureteric orifice and intravenous injection of indigo-carmine had not given any evidence of the dye coming from the right side within twelve minutes, while it appeared from the left kidney within normal time. Pyelography was not carried out. *Bacillus coli* was found, on culture, in the urine.

The second specimen I removed from a woman aged 60, who had been passing blood in her urine for a week and who made a good recovery. It shows worm-like masses of blood-clot in the pelvis and the upper calyces (fig. 3). In the cortex, towards the lower pole, there is a rounded mass of new formation, bulging on to the outer surface. The section of this area, on naked-eye examination, had the appearance of a localized inflammatory focus. Microscopically this was confirmed. The state of dilatation of the kidney itself shows a predominance of the distension in the pelvis over that of the calyces. The commencement of the ureter is kinked and, after freeing the adhesions, it was found that it was the seat of a stricture.

When I first saw the patient, her general appearance was beginning to show evidence of loss of blood. Physical examination gave no indication as to the source of the bleeding, nor had the patient made any complaint of pain. On cystoscopy one saw blood pouring from the right ureteric orifice, while the injection of intravenous indigo-carmine showed a normal functional activity of the left kidney, but no evidence of excretion of dye from the right. A plain skiagram failed to reveal the presence of stone while descending pyelography showed clearly the hydronephrosis on the right side, with a normal kidney on the other. *Bacillus coli* was found, on culture, in the urine.

My third specimen I removed from a boy aged 11, who also made a good recovery. The kidney is seen to be an old-standing hydronephrosis. On opening the renal substance, an area of extravasated blood was found in the atrophied renal tissue which on microscopic examination had all the appearances consistent with traumatism.

The ureter is seen to be firmly compressed by the normal inferior branch of the renal vein. The pelvis has slipped forward over the inferior branch of the blood-vessel, dragging the ureter with it, so that ultimately the latter is considerably compressed. The boy had fallen on his abdomen while running along in a park. The accident was followed several hours later by hæmaturia, which had been present for three days when I first saw him. Physical examination revealed a cystic swelling in the left renal region. The tumour was large and easily palpable, so much so that it was obvious that it must have been pre-existent to the accident which precipitated

symptoms. On going further back into his history, at this stage, it was ascertained that since the age of two he had suffered from recurring attacks of pain in the left side, which were sometimes accompanied by vomiting. These facts confirmed the

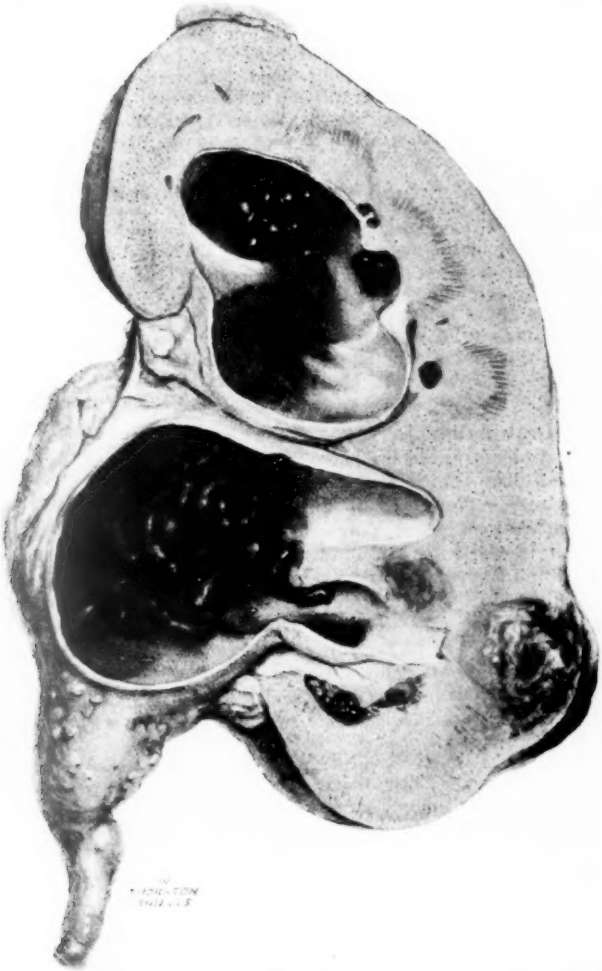


FIG. 3.—Infected hydronephrosis with abscess in cortex and blood-clot in pelvis.

suspicion that the fall had caused some traumatism to a pre-existing hydronephrosis. Descending pyelography confirmed this diagnosis by showing a normal kidney on the right side and only a faint, diffuse increase in density on the left.

Discussion.—THE PRESIDENT said that, some years ago, Mr. Winsbury White had shown that the posterior-inferior branch of the renal artery was not the cause of these cases of hydronephrosis, and nobody could say what was the cause. Sir John Bland-Sutton had suggested that it was inadequacy of the ureters. These cases had been seen with the vessel kinking the ureter, but, apparently, that was a secondary effect.

He congratulated Mr. Winsbury White on being able to do a partial nephrectomy. He had had two cases of the kind in recent years, both hydronephroses of the lower half, but in neither of these would it have been possible to do a hemi-nephrectomy; the pelves overlapped, and one could not remove the lower part without damaging the upper part; he thought the distribution of the vessels would usually prevent the procedure.

Mr. RICHES said he did not think infection or injury was the cause of hæmaturia in all cases of hydronephrosis. He had a case in which there had been hæmaturia for some months, and which showed all the effects of loss of blood. On cystoscopy blood was found to be pouring from the right side, and he (Mr. Riches) had performed nephrectomy the same day. There was little renal tissue remaining; the whole pelvis was filled with blood-clot and was studded with firm, irregular nodules, which he was unable to interpret macroscopically, but microscopically they were seen to be fibrinous masses resulting from previous bleedings.

Mr. E. T. C. MILLIGAN said he had had a case similar to that described by Mr. Riches, and had recorded it at a meeting of the Section as a massive hydronephrosis. The patient had not sought advice on account of the size of the tumour or of pain, but because of the bleeding. A small stone was found, which was not the cause of the bleeding.

Mr. WINSBURY WHITE (in reply) said that the specimens which he had collected showed that there were a number of causes of hydronephrosis. He had a specimen showing marked stenosis of the outlet of the pelvis, so that only a bristle would pass. He had another specimen showing a definite stricture of the ureter just below its junction with the pelvis. There was also the type in which the ureter was markedly kinked, and the kink was adherent to the pelvis. Those were three kinds of demonstrable causes. There was, however, a group which defeated him, i.e., the hydronephrosis without any apparent cause.

Granuloma Inguinale.—E. T. C. MILLIGAN, F.R.C.S.

This is a case of ulceration of the penis, and I cite two similar cases. Sometimes the ulceration is so deep that it almost cuts the penis in half. It may extend to the pubic and inguinal regions. It is a simple ulceration with a clean base; the edges are not undermined. The diagnosis lies between granuloma inguinale and some form of syphilitic or tuberculous ulcer; it is often mistaken for carcinoma. In one case excision was carried out, and ulceration began again at the excised part. It has not responded to anti-syphilitic remedies. There are usually found Leishman-Donovan bodies but I have not succeeded in finding these in this case. I have used another test, i.e., the effect of tartar emetic on the ulceration; after a few doses the ulceration ceases and the part heals. It is not contagious, for a man can live with his wife for months without her having the condition.

Discussion.—Dr. F. PARKES WEBER said that this condition was rare in England, but he had seen one or two cases.

In 1913, Durand, Nicholas and Favre, of Lyons, described a disease (chiefly of the inguinal lymph-glands), sometimes called "the fourth venereal disease." It was seen in subtropical countries, and cases of it had also been found in France and other Continental countries. In France it was known as "poro-adénite granulomateuse"; "poro" in consequence of the little pores full of pus which were seen on section of the affected lymphatic glands. Did English doctors call the condition that Mr. Milligan now showed "inguinal granuloma," and by what name did they know the "poro-adénite" of the French?

Mr. HOPE CARLTON said that this was a common condition on the West Coast of Africa and in the Southern States of America. Three months ago he had had a typical case of granuloma inguinale. No Leishman-Donovan bodies were found. He had discussed the case with Dr. Hanschell, who said that there were two forms of the disease: one in which there were Leishman-Donovan bodies, and another in which they were not found. On the former, tartar emetic acted like a charm. About the second form he consulted the Radium Institute, and was told that radium was of no use for the condition. He thought the condition in the present case was "poro-adénite."

Mr. R. S. ROPER said that in a case he had seen at King's College Hospital, there was a small, dry, indolent ulcer of the penis. It was thought to be venereal but the Wassermann reaction was negative. The use of tartar emetic was suggested and the condition had cleared up at once. There were no enlarged glands. The patient had lived in America some years.

Mr. MILLIGAN (in reply) said he was sure that the term "granuloma" was a misnomer; there was no resemblance to granuloma. The glands were never infected in this disease; they did not swell, and there was no pus in them. He found that this patient had had sexual connection in France two weeks previously.

Clinical Section.

President—Mr. CECIL P. G. WAKELEY, F.R.C.S.

[*December* 12, 1930.]

Bronzed Diabetes.—GEOFFREY EVANS, M.D.

A man, aged 59, a labourer, was admitted to St. Bartholomew's Hospital under the care of Sir Thomas Horder, complaining of giddiness and abdominal pain.

History of abdominal pain, having no relation to meals, and of vomiting in morning before breakfast, five years ago. At same time noticed a "brown discoloration," first of face and later of hands. Four years ago, loss of appetite; a year later, pains in calves of legs and in arms, and attacks of giddiness for which he was treated in hospital. Two years ago liver was found to be enlarged, and patient still complained of abdominal pains. Fifteen months ago, increasing weakness of left arm and hand, first noticed eighteen months previously. Four months ago, as result of attack of giddiness, fell into the docks and was admitted to hospital.

Past history.—At age of 16, urethral discharge; at age of 33, typhoid fever.

Habits.—Alcohol: three or four pints of beer daily, recently less.

Patient's colour is a greyish-leaden hue; he is somewhat emaciated. Heart and lungs natural. Liver extends five fingers' breadth below costal margin down to level of umbilicus in nipple line; edge hard and rather sharp; surface a little irregular. Spleen felt two fingers' breadth below costal margin on deep inspiration. No ascites. Rectum normal. Urine normal.

The interest of the case is partly due to the fact that a diagnosis was obvious from the patient's facies, and was confirmed, in spite of the absence of glycosuria, by the subsequent demonstration of reduced sugar tolerance and the removal of a small piece of skin which showed deposits of iron-containing pigment.

Blood-sugar curve 6.8.30. Points for curve: (50 grm. dextrose).

	Blood-sugar mgm. per 100 c.c.	*Glycosuria* Qualitative	*Ketonuria*	*Volume of Urine*
Before dextrose	101	Very slight trace	0	12 c.c.
½ hour after	172	—	—	—
1 ,, ,,	231	—	—	—
1½ ,, ,,	229	—	—	—
2 ,, ,,	180	Slight trace	0	65 c.c.

"Fasting level normal, but subsequently curve is raised and prolonged. A result which would be expected in hæmochromatosis" (signed G. A. Harrison).

Section of skin.—There are small deposits of pigment (containing free iron), presumably hæmosiderin, in the connective tissue around the sweat glands and sebaceous glands. There is no excess of melanin pigment. The condition is as seen in early hæmochromatosis. Test of stools for occult blood, negative. Skiagram of stomach and intestine showed no abnormality. Electrocardiogram normal.

URINE REPORTS.

(*Dulwich*).

	9.11.30	*10.11.30*	*11.11.30*	*12.11.30*	*13.11.30*
Specific gravity	1028	1026	1028	1028	1026
Reaction	Acid	Acid	Acid	Acid	Acid
Sugar	Nil	Nil	Nil	Nil	Nil

	14.11.30	*15.11.30*	*16.11.30*	*17.11.30*
Specific gravity	1028	1028	1026	1028
Reaction	Acid	Acid	Acid	Acid
Sugar	Nil	Nil	Nil	Nil
Bile		Nil		

(*St. Bartholomew's*) :—1020, acid, no albumin, no sugar, no blood. Diastase in urine.

Blood-count 30.7.30.—R.B.Cs., 4,730,000; Hb., 70%; C.I., 0·74; W.B.Cs., 5,600.

Differential count on 4,800 cells.—Polys. 41%; lymphos., 50%; large monos., 5%; eosinos., 2%; basos., 2%.

Blood Wassermann reaction ++

Hæmochromatosis, with Diabetes Mellitus, Hepatic Cirrhosis and Chronic Ascites.—F. PARKES WEBER, M.D.

The patient (A. P.), aged 54, an English picture-frame-maker, was admitted to hospital on November 4, 1930, in a somewhat drowsy state. The skin of his whole body was rather dry, and showed slight "slaty" pigmentation. There was moderate ascites and the liver and spleen both reached down to umbilical level. His urine was of specific gravity 1035; acid; free from albumin; it contained 4·6 per cent. sugar, much acetone and diacetic acid, but was free from indican and excess of urobilinogen. Brachial blood-pressure: 115/70 mm. Hg. The blood-serum showed no lipoid turbidity; contained 150 mgm. per cent. cholesterol (within normal limits); and gave a very slightly positive indirect (negative direct) Hijmans van den Bergh reaction and negative Wassermann and Meinicke reactions. Blood-sugar (November 11): 0·230 per cent. Nothing abnormal by ophthalmoscopic examination. The blood sedimentation rate is slightly accelerated as compared to the normal average. The blood-picture (November 21) shows nothing special, excepting that in the differential count the lymphocytes are 31 per cent. and there are 7 per cent. eosinophils. The treatment is by insulin and tapping the ascites when required. It seems that the present illness was first noticed about four months before admission, when the patient commenced to pass more urine than he was wont to, and some darkness of his skin was observed. He had been under insulin treatment before admission, but nevertheless for two months he had been troubled with thirst. Previously he seems to have enjoyed good health, but had malaria 12 years ago, and pneumonia once when younger. Has apparently been a moderate beer-drinker.

Dr. Weber thinks that visceral without cutaneous hæmochromatosis may be present in some cases of hepatic cirrhosis with diabetes mellitus, even when there is no cutaneous pigmentation.

Discussion.—Dr. PARKES WEBER added that his case was very similar to that shown by Dr. Evans, but the slaty colour of the skin was slightly less. It resembled one of the cases shown at the last meeting of the Medical Section of the Society (at Guy's Hospital). Moreover, the cirrhosis of the liver in his case had already caused ascites, which had constantly to be tapped. The speaker desired to emphasize that the typical coloration in hæmochromatosis was usually not bronze as the name "bronzed diabetes" would imply, but slaty, and there might sometimes be a blue tinge in it. One of the earlier carefully-examined cases was that described by Dr. Maude Abbott, and the patient had been known in the ward of the hospital as "Blue Mary" on account of her slaty-blue appearance.[1]

Dr. BERNARD MYERS asked whether there was any appearance of carotinæmia in these cases.

Dr. PARKES WEBER (in reply) said that cases which had shown no obvious pigmentation during life had sometimes been diagnosed post-mortem by the presence of hæmochromatosis in the liver and viscera. Clinically, when marked diabetes mellitus was found associated with obvious cirrhosis of the liver, hæmochromatosis should be suspected even if the skin showed no pigmentation. In answer to Dr. Bernard Myers, there was nothing in the present case to suggest any excess of lipochrome or carotin-like pigment (no xanthosis of the palms of the hands or soles of the feet).

[1] M. E. Abbott, *Trans. Path. Soc. Lond.*, 1900, li, p. 66.

Calcified Endothelioma of the Brain Seven Years after Decompression.—CECIL P. G. WAKELEY, F.R.C.S.

T. F., male, aged 40, admitted to King's College Hospital, October, 1923, because his left leg was "giving way." Had attacks of faintness and giddiness and occasional severe headache, sometimes accompanied by vomiting.

On examination.—Eye movements normal. Pupils equal and reacted to light and accommodation. Vision: right $\frac{6}{9}$; left $\frac{6}{9}$. Right fundus: Definite papillœdema, with complete obliteration of disc and arteries, which were almost entirely obliterated. Veins showed considerable distension. Best seen with + 7 D. Left fundus: Condition similar to right. Best seen with + 6 D. Both fields seemed quite normal.

Patient mentally bright, responded quickly, answered questions and gave a good account of his condition.

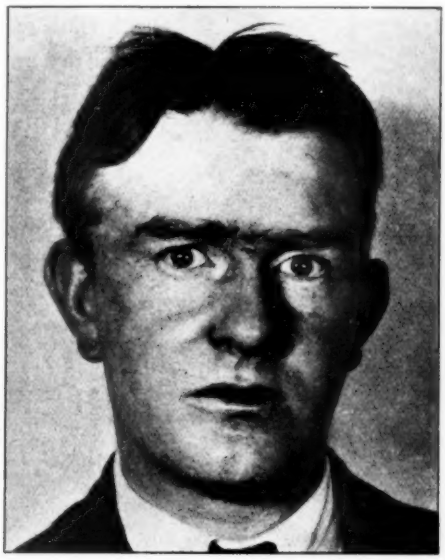


FIG. 1.—Photograph taken in December, 1930, seven years after right subtemporal decompression. There is very little bulging of the brain through the opening.

Reflexes normal on both sides. Plantars flexor; left abdominals tired more rapidly than right. Wassermann reaction negative in blood and cerebrospinal fluid. Skiagram of skull demonstrated calcified tumour in region of third ventricle.

Right subtemporal decompression performed October 24, 1923. The calcified tumour could be felt 2½ in. internal to cortex of brain. Any pressure on the tumour caused marked fall of blood-pressure and cessation of breathing. Wound closed. Patient made excellent recovery and has been at work ever since.

From 1925 to 1929 had several attacks lasting a few minutes only.

Present condition.—Complains of occasional frontal headaches when tired. Left foot drags when he walks, and the dragging is becoming worse.

Eye movements and reactions normal. No nystagmus. No sign of papillœdema. No optic atrophy. Discs healthy colour. Vision: Right $\frac{6}{6}$; left $\frac{6}{6}$. Field of vision normal.

Some weakness of left seventh cranial nerve. Other cranial nerves normal. Some spasticity of left arm. Left grip weaker than right. Supinator, biceps- and triceps-jerks brisk, and on left side definitely increased.

Abdominal reflexes.

Right	*Left*
present	absent
absent	present

Left leg spastic. Knee- and ankle-jerks brisk on right side and definitely increased on left., No ankle clonus. Extensor plantar responses on both sides. Sensation unimpaired over whole of body.

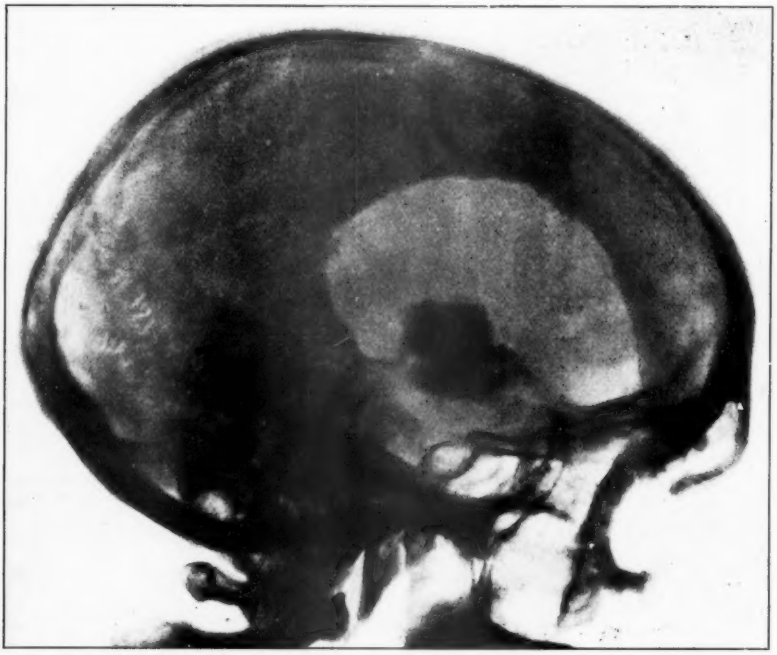


FIG. 2.—Lateral skiagram taken in 1930, seven years after the operation. The tumour can be readily seen.

Decompression area is soft; underlying brain can be felt pulsating.

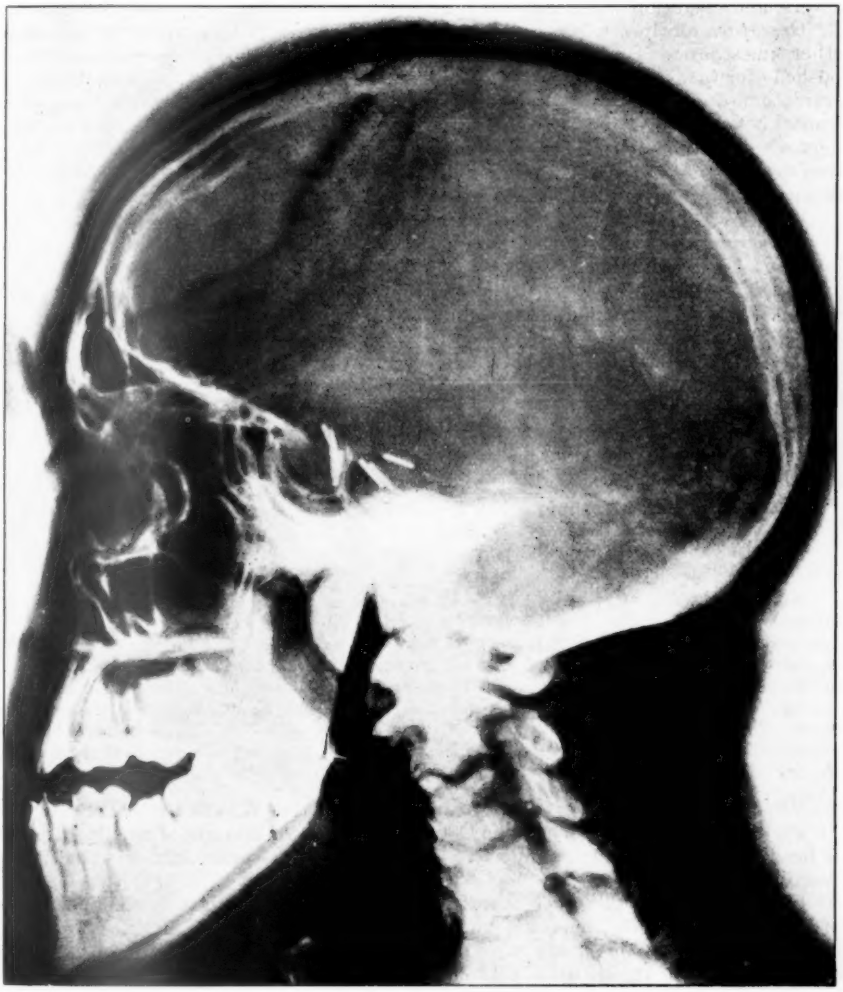
Skiagrams taken by Dr. Graham Hodgson show position of the tumour extremely well.

The patient has come up to hospital because hemiplegia has developed. The skiagram shows a calcified tumour just behind the wing of the sphenoid (fig. 2). Since 1923 it does not seem to have increased, but the density appears to be a little greater; this, however, may be due to the X-ray films, which have improved in quality during the last five years. The patient is employed in the Civil Service, and notwithstanding a slightly shuffling gait, he is able to do a full day's work.

Acromegaly Treated with Radon Seeds. — CECIL P. G. WAKELEY, F.R.C.S.

I. W., female, aged 21, admitted to hospital, 30.10.30, complaining of headaches, which began two years ago, after gastric influenza. She was then ill for three months. For three weeks she had a high temperature, and vomited all food. After this illness headaches began to develop and have slowly become worse; lately they have been entirely left-sided, with pain in left side of neck, and left ear.

During the past six to nine months, patient has been growing a great deal; whole body seems to have grown, but especially hands and feet. Clothes bought three



Lateral skiagram showing radon seeds in situ. The position of the osteoplastic flap in the frontal region can be seen.

months ago will now not nearly fit her. Her back and limbs ache a great deal, and she easily becomes tired. She was fitted with glasses on account of the headaches, but these only gave temporary relief. Sight is good, but concentration on reading seems to get on her nerves; the words appear to come up to her eyes, so that she has to throw down the book or newspaper.

Has been growing very irritable for the last three months. Wants to sleep at odd times. Drinks pints and pints of water. Polyuria. Menses, every six weeks. Hair not falling out. Thyroid gland somewhat enlarged, but difficult to be certain of this, owing to thickness of neck. Sweats a great deal. Wassermann reaction negative. Skiagram showed a very large pituitary fossa. Headaches became more severe, and operation was decided upon.

Operation for insertion of radon seeds performed 7.11.30, under intratracheal ether anæsthesia. Scalp incision made from ear to ear across vertex and scalp pushed forwards over supraorbital ridges. Large bone-flap cut with Souttar's craniotome from right frontal region. Dura mater stripped from orbital plates of frontal bone, and then incised just in front of small wing of sphenoid. The optic nerves were exposed, and a small tumour of the anterior part of the pituitary body was seen. Nine radon seeds were inserted round about the tumour. Bone flap replaced, and scalp sutured with interrupted silkworm gut sutures.

Uninterrupted recovery; headaches completely disappeared.

Skiagrams (Dr. Graham Hodgson) show radon seeds in position, and demonstrate position of osteoplastic flap.

I was tempted to remove the tumour, but thought it better to treat it with radon, because I have had better results with radon seeds in these cases than by operation. The patient is perfectly well to-day (five weeks after the operation). A curious thing about these cases treated with radon seeds is that during the first fortnight of treatment the papillœdema becomes more marked. Mr. Cargill reports that the eyesight was normal. It is rather interesting that polyuria sometimes occurs after the introduction of radon seeds, while a patient who has had polyuria, owing to the pituitary tumour, may be absolutely cured, as in this instance, by the introduction of radon seeds.

Dr. F. R. B. ATKINSON referred to the publication in the literature of cases in which radium treatment had been used in preference to surgical removal. Why had Mr. Wakeley thought it better to undertake an operation to insert the radon seeds rather than to use radium intranasally?

Mr. WAKELEY (in reply) said that he had always been reluctant to operate on the pituitary intranasally, because it was rather difficult, and one could not see what one was doing, so that it seemed a somewhat haphazard method of application. If radium was used, it had to be removed at a later date, and this required another operation, whereas radon seeds were left in situ permanently. By the intranasal method, it could not be determined, when one went through the sphenoidal sinus, whether the seed was in the tumour or in part of the pituitary itself. When the anterior lobe was enlarged, the posterior lobe might be coming forward underneath, so that one might be putting the radium into that and not even near the tumour. He, therefore, always preferred the frontal approach with regard to these pituitary tumours.

Vascular Tumour of the Brain.—CECIL P. G. WAKELEY, F.R.C.S.

Patient, A. W., previously shown October 10, 1930,[1] on account of swelling at back of head, gradually increasing in size. Photograph shows exact size and position of swelling.

Operation 17.10.30, under intratracheal ether anæsthesia. Semicircular flap of scalp turned down, exposing the tumour. Hæmorrhage controlled by scalp forceps. Small trephine made in skull, about an inch above tumour. Opening was enlarged until it fused with pathological opening in occipital region. Superior longitudinal sinus exposed and packed with gauze. Tumour mass—friable, vascular, and dark in colour—removed with spoon from outer side of dura. There was

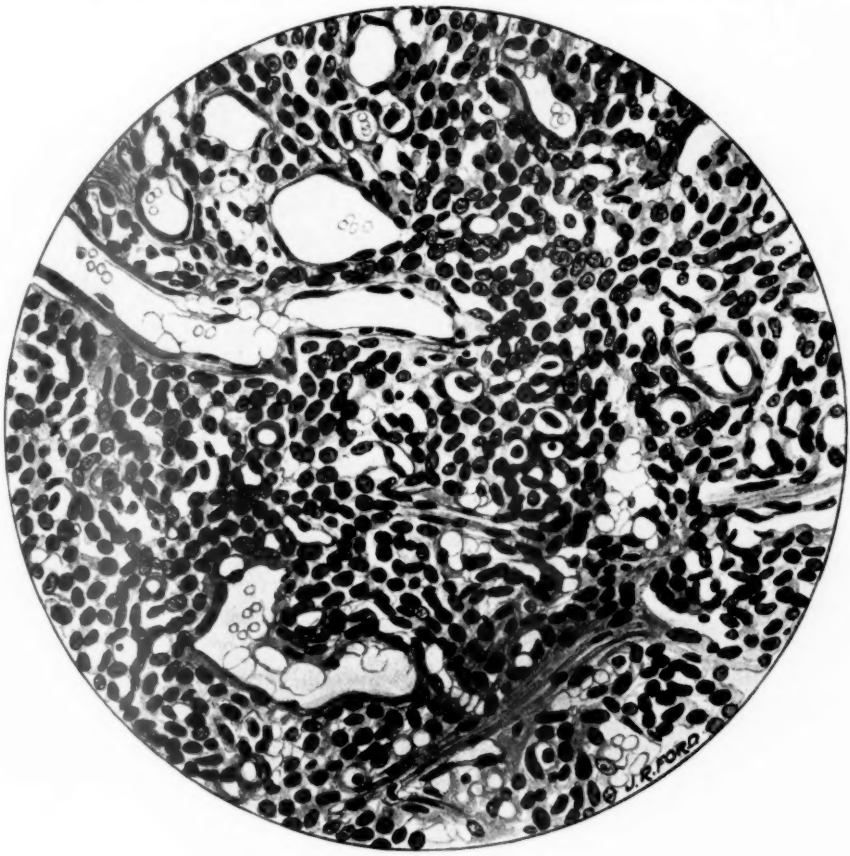
[1] *Proceedings*, 1930, xxiv 65 (Clin. Sect., 5).

excessive bleeding, and the whole cavity had to be packed with gauze. The scalp was sutured with thick interrupted silkworm gut sutures. Plugging removed two days later under general anæsthesia.

Headaches disappeared, as also did the whistling murmur previously present.

7.11.30. Pastille dose of X-rays given to region of tumour.

Microscopical Report on Tumour.—The tumour is an endothelioma, probably arising from vascular endothelium. It is very cellular, and the cells tend to be massed together with very little cytoplasm, so that their shape cannot be



Microscopical drawing of the tumour × 350.

made out. The nuclei are large and vesicular, and have well-marked nucleoli. Vessels, probably blood-vessels, are present in large numbers. Many have an endothelium distinct from the tumour, but others appear to have an endothelium which passes without any line of demarcation into the tumour masses themselves.

Dr. PARKES WEBER said that in the previous discussion on this case, one of the questions raised was whether the tumour might have been a kind of racemose meningeal angioma. But nobody present at the meeting had ever heard of such an angioma, which

had perforated through the skull and produced a spontaneous decompression. The diagnosis of hæmangio-endothelioma was brought up, but because the tumour had perforated through the skull, the idea suggested itself that it must be malignant, and that the usually endotheliomatous part of the hæmangioma was sarcomatous. That was why he (Dr. Weber) had suggested that it might be a hæmangiosarcoma.

Headache Relieved by Removal of a Portion of Middle Turbinal Body.—Sir JAMES DUNDAS-GRANT, K.B.E., M.D.

A young woman medical student complained of left frontal headache from which she had suffered from time to time since childhood, especially after exposure to cold or sea-bathing; it was always accompanied by extreme stuffiness of that side of the nose. Attacks were intermittent and generally relieved by administration of veramon. In September, 1929, after patient had been camping and sea-bathing, headache occurred nearly every morning with considerable intensity. After removal of portion of left middle turbinal, pain disappeared and severe coryzal attacks ceased; patient was able to take cold baths without nasal stuffiness. This year, after summer camping and sea-bathing, the pain recurred and a further portion of the left middle turbinal was removed, with the result of complete freedom from pain. At the time of operation the insertion of a firm plug in the nose awoke the pain for the moment, suggestive of the causation.

Frontal Headache Relieved by Removal of Portion of Middle Turbinal.—Sir JAMES DUNDAS-GRANT, K.B.E., M.D.

A man, aged 25, carpenter, complained of pain over left eye, of three years' duration, worst at about eleven o'clock in forenoon. Left antrum had been operated on, and on transillumination was only slightly less clear than other sinuses. Some enlargement of the middle turbinal on the right side, but on the left side a slight deflection of the septum pressed on an enlarged middle turbinated body. I removed the redundant portion of the left middle turbinal the day after I first saw the patient, and from that time he was free from his headache.

Presumably there had been catarrh of the frontal sinus and the escape of secretion had been obstructed by pressure of the middle turbinated body on the outlet. The periodical recurrence of the pain in the forenoon is rather characteristic of frontal sinus catarrh; the pain is attributable to the vacuum occasioned by the gravitation of the contained fluid some hours after the patient has assumed the vertical posture.

Frontal Headache Relieved by Submucous Resection of the Nasal Septum and Removal of Redundant Portion of Middle Turbinal.—Sir JAMES DUNDAS-GRANT, K.B.E., M.D.

A youth, aged about 19, first seen September, 1930, complained of frontal headache coming on each day at 11 a.m. and lasting till about 4 p.m. He had the appearance of great suffering. There was slight tenderness over the left frontal sinus with deflection of the septum to left, coming in close contact with the left middle turbinal. Radiologist reported that nasal sinuses were less translucent on left side than on right. After submucous resection of deflected portion of septum and removal of redundant portion of left middle turbinal, pain disappeared. Patient looked a different man and subsequently reported himself free from pain.

Sir JAMES DUNDAS-GRANT, in reply to a question, said that the periodical recurrence of pain some hours after the patient had assumed the vertical posture was seen so often that the vacuum occasioned by the gravitation of the contained fluid must be one explanation of it, even if it was not the only one. Thus, the air in the sinuses was likely to be absorbed, and a vacuum thereby formed some time after rising. The fact of frontal pain coming on at the same time pointed to a frontal sinus catarrh. It was certainly

an observation made frequently by many rhinologists. One young man was about to have this operation done, but by the use of an ointment consisting of adrenalin and anæsthesin, he was so much relieved that he thought he could get along without any further operation.

Syndrome of Obliterating Arteritis of the Lower Limbs treated with Angioxyl and various Physical Agents. — A. P. CAWADIAS, M.D., and F. PARKES WEBER, M.D.

G. T. G., male, aged 42.

Since 1927, intermittent claudication; no definite diagnosis. About August, 1929, noticed small sore between fourth and fifth toes of left foot, and in March, 1930, the little toe, which had been gangrenous for some time, dropped off. Admitted to German Hospital. Diagnosis: arterial obliteration localized in left lower limb (F. P. W.). Patient has intense spontaneous pains. Wassermann reaction negative.

On examination.—Limbs cold, particularly left. Pulse of arteria dorsalis pedis felt very faintly in April, 1930.—Oscillometric exploration: Oscillometric index left leg, 1½; left thigh, 2½; right leg, 3; right thigh, 6.

May, 1930, had attack showing features of angina pectoris. Stayed in bed for a few days, but attacks of præcordial pain continued.

Treatment begun June, 1930. Injections of angioxyl, two or three per week. Local irradiation of limbs with ultra-violet rays and diathermy; later, local irradiation with infra-red rays. After three months of treatment condition greatly improved; spontaneous pain disappeared. Intermittent claudication rare, occurring only on over-exertion. He even danced one evening for two hours.

Condition retrogressed slightly at beginning of September, but after series of more frequent injections and treatment, patient was again quite well. No spontaneous pain; walking easily; intermittent claudication is exceptional. Oscillometric exploration (November 29, 1930) shows distinct diminution of the arterial obliteration. Oscillometric index: left leg, 3; left thigh, 4; right leg, 5; right thigh, 6.

Discussion.—Dr. S. LEVY SIMPSON said that oscillometry was of much value in quantitative diagnosis, but its use as a therapeutic index was often fallacious. The amplitude of pulsation depended not only on the local condition of the artery, but also on the state of the general circulation at the time of examination, a factor which was obviously variable. The surface temperature was of far greater value as a therapeutic index.

Dr. PARKES WEBER said that he agreed with Dr. Cawadias that endarteritis proliferans obliterans was the condition which would most probably be found microscopically in this case, if the affected arteries could be examined. But he felt that the typical cases of thrombo-angiitis obliterans, described by Leo Buerger, were not quite the same. He thought that in those cases thrombosis was the main histological feature of the obliteration of the affected vessels and that proliferating endarteritis was so uncertain and so small a factor that the balance of evidence was that thrombo-angiitis obliterans ("Buerger's disease"), whether in Jews or in Gentiles was a different disease. Dr. Parkes Weber added that by "proliferating endarteritis" he meant the same pathological process as arterial atheroma and arteriosclerosis, when the endarteritis occurred in the absence of specific causes, such as syphilis.

Angioxyl could not of course be expected to have a like good effect in all cases. Dr. B. Barling had intended to bring up a case in which angioxyl had relieved the pain when tried before peri-arterial sympathectomy, but when tried again after that operation, it failed to relieve pain.

The PRESIDENT said he agreed with Dr. Levy Simpson that the most important thing in these cases was the surface temperature. He had had a diabetic patient, with gangrene of two toes; the dorsalis pedis artery could not be felt. As the patient would not allow amputation, peri-arterial sympathectomy was carried out on the common femoral artery.

and within three hours of the operation the surface temperature of the foot was raised by 3°. At the end of a week it remained 6° or 7° higher than before the operation and afterwards the two toes dropped off and the gangrenous patch cleared up.

Dr. CAWADIAS (in reply) said that the oscillometric exploration of the arterial permeability was absolutely necessary for an early and precise diagnosis of arterial obliteration of the limbs. The diminution of the oscillometric index characteristic of arterial obliteration took place long before any distinct modification of the pulse of the arteries, and thus by applying the oscillometric method in all doubtful cases, an early diagnosis could be made and treatment could be applied at a period in which it was really effective. In France the oscillometric method of the arterial permeability is a routine method. It was indifferent which oscillometer was used but in his (Dr. Cawadias') experience, Pachon's oscillometer was superior because it combined constancy of results with extreme sensitiveness.

The method of taking the surface temperature could not be compared with the research of this oscillometric index. Surface temperature of the limbs indicated the condition of the capillaries of the skin; oscillometric index indicated the condition of the lumen of the artery —two absolutely different things. The research of the oscillometric index was not only necessary for early and precise diagnosis, but it also indicated the progress of the condition. There were of course normal variations of the oscillometric index in the course of the same day for the same subject, but these variations did not exceed $\frac{1}{2}$ or 1 division of Pachon's oscillometer and this could not disturb the general results.

Angioxyl was not, of course, the only factor in the treatment of these conditions, but must be combined with other methods—especially physical ones. It was, however, an extremely important agent because it corrected the metabolic disturbances at the base of the arterial obliterations. Seeing that patients—though in an advanced stage of the condition in which gangrene had begun—had been cured by purely medical methods, he (Dr. Cawadias) thought that in such cases we should be very conservative and avoid surgical operations except when there was definite and extensive gangrene.

Hyperparathyroidism: Generalized Osteitis Fibrosa with Multiple Osteoclastomata.—DONALD HUNTER, M.D.

M. F. R., single woman, aged 37.

History.—Born in Greenwich. Employed in post office from 1908 (when aged 15) till March, 1928.

Summer, 1925.—While on holiday (chiefly walking) along Rhône valley had slight injury to right foot making the arch painful for a few weeks. Continued to walk and was otherwise well.

May, 1926.—Slight pain in knees, hips, heels, and in arms. Weakness and lack of energy. Unable to walk any distance; had to give up tennis but was able to work. Occasionally cried with pain on shaking hands.

May, 1927.—Seven weeks' holiday on account of pain in legs and knees.

September, 1927.—Pain much worse in hips, knees, and heels. Legs and thighs unaffected. Pain never prevented her from sleeping, was worse when she moved about. In bed for seven weeks. Temperature was normal, but she was thought to be suffering from rheumatism. Pain and weakness occurred in the arms, and she had to give up work because she could not stoop or lift the heavy ledgers.

February, 1928.—Hardly able to get about because of pain and weakness. Unable to get up from a chair or to walk with aid of a stick. Slight swelling of jaw was noticed. Right hip was now the site of worst pain. Improved slightly, went back to work half-time for two months.

March, 1928.—Had to leave work permanently.

June, 1928.—Slipped from her chair and was doubled up at the hips. Had to be lifted up and has not walked since. Great stiffness of lower limbs, hips becoming very painful and knees remaining straight. Admitted to Greenwich and Deptford Hospital, where she remained in bed for five weeks. While under treatment she noticed a swelling of the left forearm and another on the back of the right hand. Mercury ointment was rubbed into these without effect. Radiograms taken of

jaw and of both hip-joints. She was told that there was no fracture, but that the bones were very thin. Had massage at home for three months.

October 28, 1928.—Admitted to Guy's Hospital. Weight, 5 st. 5 lb. 8 oz.

November 14, 1928.—Accidentally thrown from a wheel-chair. Painful injury of right forearm.

Radiograms of bones.—"All bones very translucent. Fracture of right radius and ulna. Shaft of left ulna shows cavitation and expansion of cortex. Ribs collapsed. Destruction of bone in third right metacarpal, both sides of mandible, necks of both femora and left iliac bone."

Urine.—Neutral. Sp. gr., 1010. Trace of albumin. Bence-Jones proteose absent. No sugar. Deposit of phosphates.

Blood-count.—Red cells, 4,460,000; white cells, 15,000; polymorphonuclears, 70%.

February 1, 1929.—Portion of tumour of mandible removed for histological section. Easily cut with a knife. Dr. G. W. Nicholson reported upon the histology: "A giant-celled epulis" (plate V).

February 4, 1929.—Serum calcium 15 mg. per 100 c.c.; plasma phosphorus 3·3 mg. per 100 c.c.

Treatment.—Right forearm immobilized in plaster for six weeks. Fractures united. Cod-liver oil given over a period of ten weeks in increasing doses, up to six drachms three times a day.

During the last seven weeks of this treatment irradiated ergosterol was given; continued for three months, dose increased to ten minims three times a day (radiostoleum). When the cod-liver oil was discontinued ultra-violet irradiation was used three times a week. Deep X-ray therapy applied to the bones (seven exposures). March 5, 1929: Left hospital.

April, 1929: Noticed swelling on inner side of right leg below knee.

May 25, 1929: Re-admitted to Guy's Hospital. Weight 4 st. 5 lb. 10 oz. Tumours of jaw and right hand larger.

Radiograms of bones.—"Heads and necks of both femora appear to be absorbed and trochanters displaced upwards. Pelvis shows collapse and absorption of bone salts, more marked on right side."

Treatment.—Four applications of deep X-ray therapy to jaw and arms. Insertion of radium into mouth. July 5, 1929: Left hospital.

April, 1930.—Re-admitted to Greenwich and Deptford Hospital. Further radiograms taken. Density of bone-shadows extremely poor. Many tumours expanding bone. Dr. Macdonald Critchley saw the patient in consultation with Dr. W. Denison Wiggins and diagnosed hyperparathyroidism.

Past history.—No history of rickets as a child. Catamenia began at age of 14; usually lasted a week. Normal until June, 1927, then somewhat excessive until June, 1928, when they suddenly ceased for eighteen months. Then irregular for six months and ceased entirely after April, 1930. In 1916 many teeth extracted for caries leaving only eleven; in 1926, eight more teeth extracted. No history of polydipsia, polyuria, renal pain, or passage of stone or gravel. In 1923, while playing tennis, fell on outstretched hand and fractured left radius. Arm was in splint for ten days and bone united within a month.

Family history.—Father, one brother and one sister, alive and well. Mother died from carcinoma of colon. No family history of fractures, dislocations, blue sclerotics, deafness, or peculiar shape of head.

May 28, 1930.—Admitted to the London Hospital.

On examination.—Height, 4 ft. 10 in. Weight, 4 st. 13 lb. Patient is intelligent and gives a concise history. Lies in bed totally disabled, deformed, frail and wasted. Hips and knees flexed. Able to move left leg but cannot straighten right leg. Unable to move either arm. Left arm aches. Great pain in right hip if she is

lifted on that side. Pressure upon the bones, especially the forearms, gives rise to pain and this is severe when she is turned in bed. Sclerotics white. Lenses normal on examination by slit lamp. Hearing normal. Tongue clean. Mucous membranes normal colour. Thyroid normal. No tumour felt in neck. Forehead prominent but skull otherwise normal. Hard, non-tender, bony enlargement on right side of mandible forming a swelling, 6 cm. in diameter (fig. 1). In the skin over it is a surgical scar. Tumour protrudes into mouth, where it is covered by bluish-red buccal mucosa. Only three teeth remain and appear to be normally calcified. Thorax tapers in upper part, superior inlet being thus reduced in diameter. Normal prominence of shoulders is missing, so that arms seem to disappear into upper part of chest, and clavicles to be too

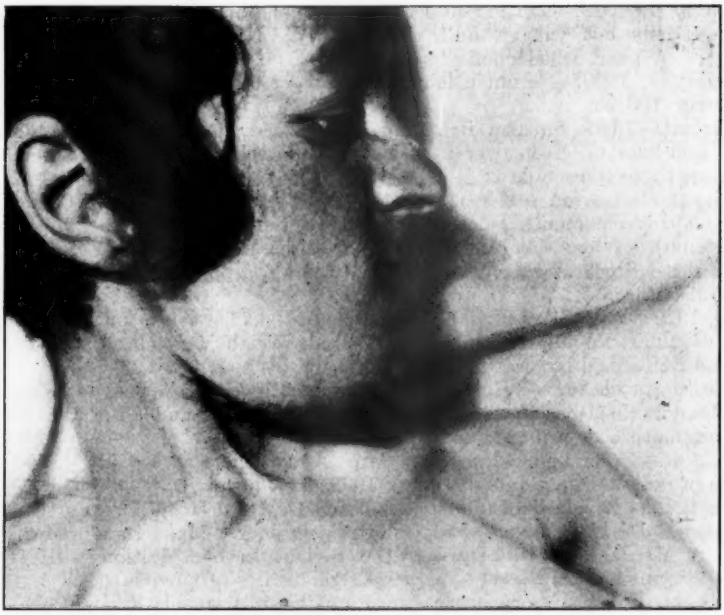


FIG. 1.—Showing bony tumour on right side of mandible.

prominent. Lower thorax widens out, subcostal angle being normal. Eight slightly tender bony nodules felt in course of ribs, especially lower ribs. Slight scoliosis. Arms extremely thin, owing to muscular wasting and to diminution in total width of bones; are crossed upon chest; range of voluntary movement limited to a few inches. Antero-external curvature of both forearms. Upper end of left ulna presents a bony swelling. Large slightly tender bony swelling 2 cm. in diameter on dorsum of right hand apparently arising in third metacarpal (fig. 2). Second left metacarpal distorted and thickened. On passive movement shoulder-joints are free, except in extreme abduction which causes pain. Free flexion of elbow-joints is possible, but not full extension. Voluntary movements of left hip and knee are good. Marked abduction of left hip and complete extension of both

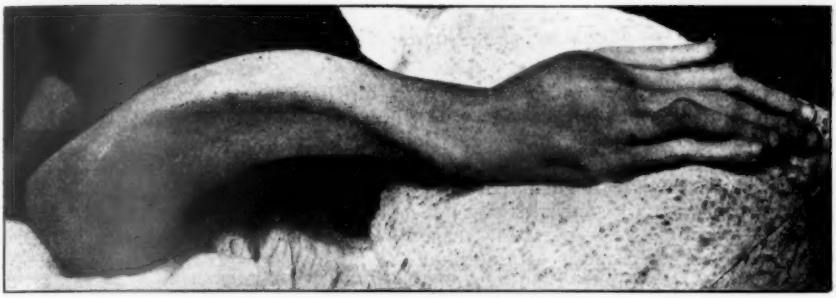


FIG. 2.—Antero-external curvature of forearm. Large bony swelling on dorsum of right hand. (June, 1930.)

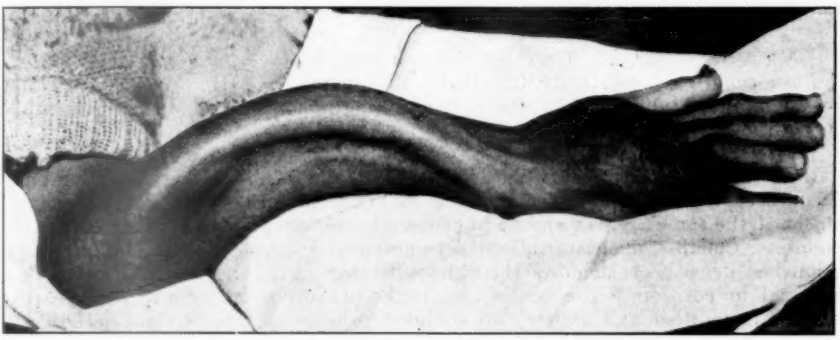


FIG. 3.—Same as fig. 2. Five weeks after operation. Swelling on dorsum of right hand has almost disappeared. (August, 1930.)

FIG. 4.—Antero-posterior curvature of upper end of right tibia and fibula.

knees give rise to pain. Movements of right hip limited. Sharp antero-posterior curvature of upper end of right tibia and fibula with its concavity forward (fig. 4, p. 43). Left lower limb not deformed. Bones of lower limbs not shortened.

Heart, lungs and abdomen normal. Blood-pressure 140/100 mm. mercury. Generalized wasting and slight hypotonicity of muscles. No abnormality in nervous system. Trousseau and Chvostek signs absent.

Urine.—Alkaline. Sp. gr., 1014. Albumin, heavy cloud. Bence-Jones proteose absent. No sugar. Deposit of amorphous and triple phosphates. Average daily output of urine (May-June, 1930) was 765 c.c.

Renal efficiency tests.—Blood-urea 0·033%.

	Phenol-sulphone-phthalein		Urea concentration
	c.c.	Percentage	Percentage
First hour ...	46 ...	28·6 ...	1·26
Second ,, ...	85 ...	16·6 ...	0·96

Blood-count.—May 20, 1930. Red cells 4,400,000, Hb. 50%, C.I. 0·55; Leucocytes 4,920; differential count normal. Bleeding time 2 minutes; coagulation time 1·5 minutes.

Wassermann reaction negative.

Radiograms of bones (plates I to IV).—Greatly diminished density of shadows of all bones examined. This is emphasized by contrast with the bones of a control subject of the same age, sex and build exposed simultaneously on the same negative. Scoliosis. Collapse of chest wall with thinning of ribs and clavicles. Extremely diminished density of shadows throughout lumbar spine and pelvis. Both hips abnormal in position. The heads and necks of both femora have disappeared. Calvaria is mottled and shows two rounded pale areas with ill-defined borders. Tumour of mandible dense and coarsely trabeculated. Head of right humerus has almost disappeared. Left humerus, right tibia, and right and left radius and ulna are bowed, frail and narrow, and showing a grossly deficient corticalis. Irregular, pale, trabeculated areas expanding the corticalis are seen in right and left ulna, in several phalanges, and in second left and third right metacarpals. The last-named is so large as to distort the adjacent second and fourth metacarpals. Fracture of second metacarpal through a pale, cyst-like area at its mid-point.

Radiograms of kidneys.—Kidney shadows normal in size. Two groups of small calculi seen in region of right kidney.

Chemistry of the Blood before Operation (Fig. 5).

	Serum calcium (mgm. per 100 c.c.)	Plasma phosphorus (mgm. per 100 c.c.)	Plasma phosphatase (mgm.)
May 19, 1930	12·1 ...	2·0 ...	—
May 26, 1930	12·6 ...	— ...	—
June 17, 1930	— ...	1·3 ...	—
June 20, 1930	11·2 ...	— ...	—
July 2, 1930	13·6 ...	— ...	1·13

Calcium output.—The calcium output was estimated in the urine and fæces over a period of nine days, during which the patient was kept on a weighed diet of low calcium content. The energy value of this diet was 1,294 calories daily. Sufficient alkali was given by mouth to make the reaction of the 24-hour mixed urine neutral to phenol-sulphone-phthalein (pH 7·3). During the nine days distilled water was used in the preparation of all her food and drinks. The fæces were divided into three-day periods by the oral administration of 0·3 gramme of carmine alum lake every third day. The urine was obtained in 24-hour specimens. The record of the calcium exchange is tabulated below, the figures being milligrammes of Ca per three-day period.

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PLATE I.

CONTROL

Controlled radiogram of right tibia and fibula.

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PLATE II.

CONTROL

Controlled radiogram of right hand and forearm.

UNIV. OF MICH.

PLATE III.

Radiogram of pelvis.

Diminished density of shadows. Abnormal position of hips. Heads and necks of both femora have disappeared.

PLATE IV.

PLATE IV.

Radiogram of skull showing mottling and rounded pale area (×).

DONALD HUNTER: Generalized Osteitis Fibrosa with Multiple Osteoclastomata.

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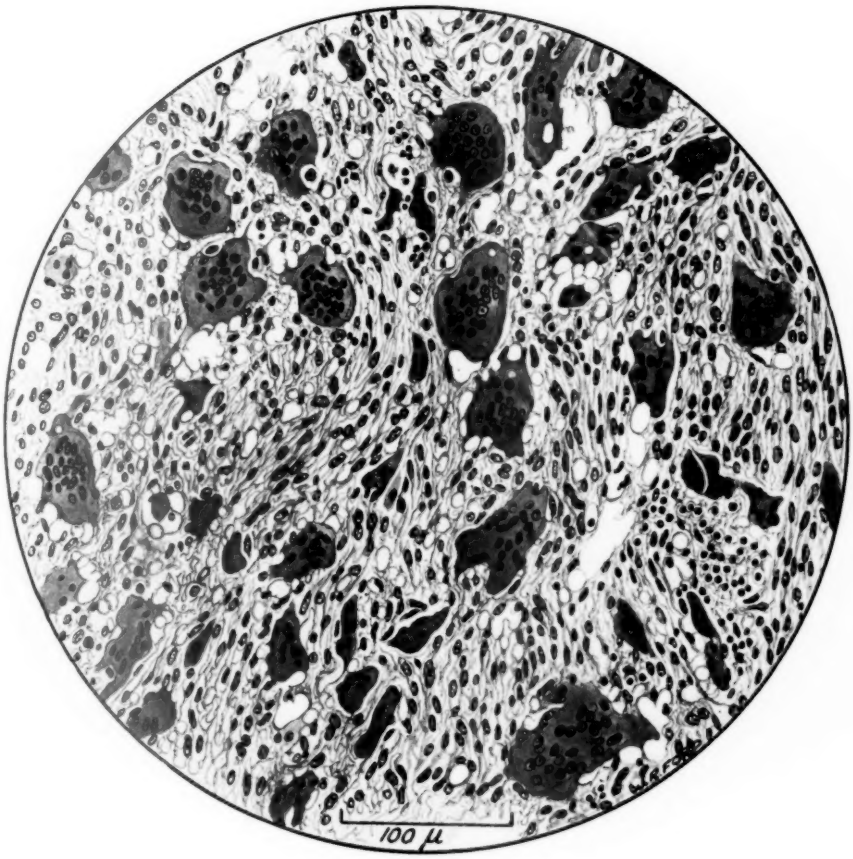
PLATE V.



Portion of tumour of mandible stained with hæmatoxylin and eosin.
(By the kindness of Dr. G. W. Nicholson.)

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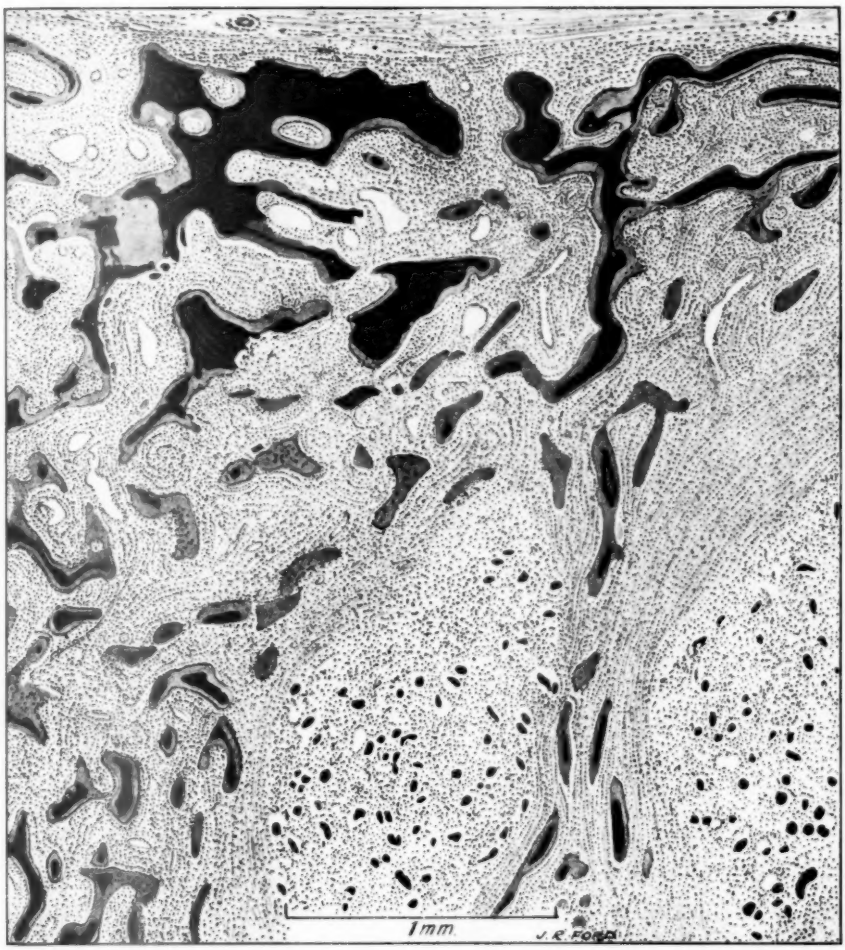
PLATE VI.



Portion of right tibia. Junction of lower, bony, segment with upper, fleshy, segment containing osteoclastomata; periosteum included. Decalcified in Müller's solution; stained with Weigert's iron-hæmatoxylin and van Gieson.

DONALD HUNTER: Generalized Osteitis Fibrosa with Multiple Osteoclastomata.

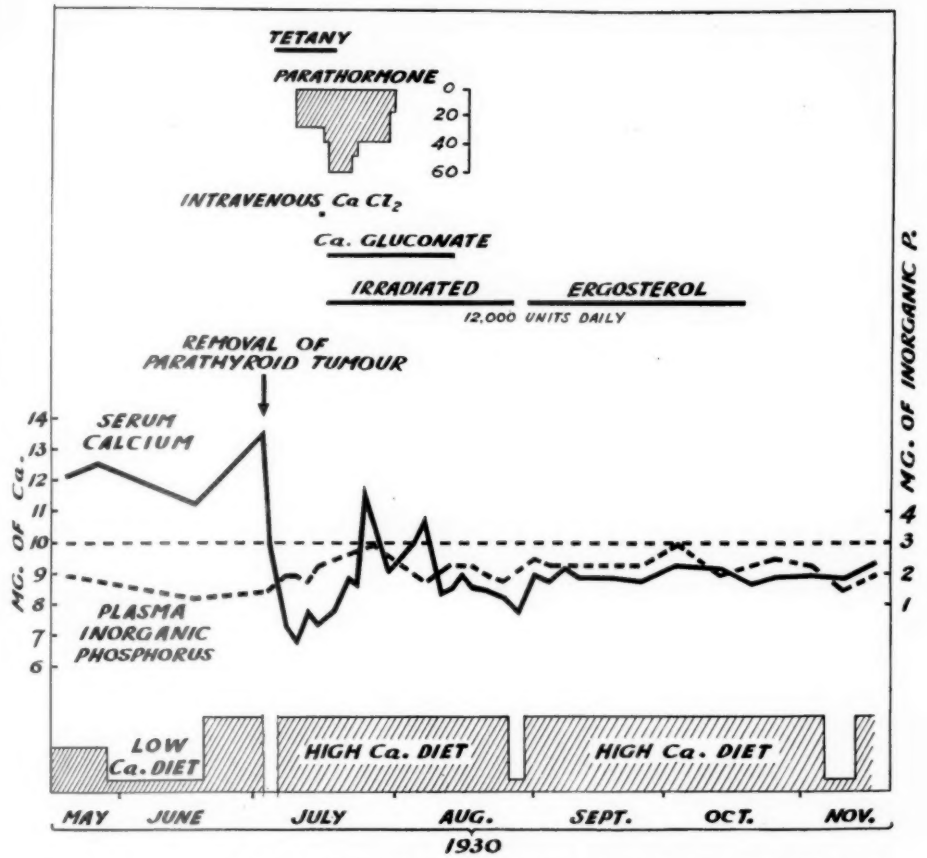


FIG. 5.—*Chemistry of the blood:* The blood was examined at intervals for two months before and for five months after operation. The low calcium diet was that given during the investigation of the calcium balance. The high calcium diet was not weighed. It included four pints of milk daily, together with ice cream, cheese and eggs. The scale indicating the dosage of parathormone represents units per day. The dosage of intravenous calcium chloride was 10 c.c. of a 5 % solution. The dosage of calcium gluconate was 10 c.c. of a 10 % solution daily, given by intramuscular injection. The dosage of irradiated ergosterol was measured in antirachitic rat units.

CALCIUM EXCHANGE BEFORE OPERATION.

Three-day Period	Calculated Intake	Output		
		Fæces	Urine	Total
I	456	240 ...	620 ...	860
II	456	200 ...	640 ...	840
III	456	290 ...	640 ..	930

Operation (Mr. A. J. Walton), July 2, 1930.—Collar incision made in neck. Sterno-mastoid muscles were retracted on either side and pre-tracheal muscles divided. Thyroid apparently normal; inferior pole of left lobe was explored, and a normal left inferior parathyroid body identified. The left superior parathyroid body, embedded in the posterior aspect of the upper pole of the left lobe of the thyroid, was

dissected out with a blunt dissector. It was enlarged and measured approximately 1·4 by 0·8 by 0·5 cm. Its blood supply was left intact. Exploration of the inferior pole of the right lobe of the thyroid failed to reveal the right inferior parathyroid body. An irregular projection from the lateral surface of the right lobe of the thyroid in its upper part was dissected out and removed. As this was completed a tumour

FIG. 6.- Tumour of right superior parathyroid (actual size).

was unexpectedly displayed projecting from behind the trachea in the situation of the right superior parathyroid body. This was a smooth, solid, oval, brown-yellow tumour measuring 2·3 by 1·5 by 0·9 cm. (fig. 6). It was removed. One drainage tube was inserted and the wound closed.

A portion of bone was removed from the upper part of the shaft of the right tibia.

PATHOLOGICAL REPORT BY PROFESSOR H. M. TURNBULL.

Tissues removed at Operation (*S.D.* 1518/1930.)

(1) *Right tibia. Macroscopic.*—The specimen was a longitudinal slice from the upper part of the shaft. It was 3·5 cm. long. The outer border was covered with periosteum. In the lower 2 cm. the cut surface was 0·6 cm. wide and consisted of a gritty, grey tissue, in which minute spicules of bone were seen with a hand-lens. It gave the impression of a closely-meshed spongiosa formed by very delicate trabeculæ. In the upper 1·5 cm. the periosteal border bulged and was easily indented with the finger nail. The cut surface was 1·1 cm. wide, and consisted of a rubbery, grey, gelatinous tissue in which no bone was seen. The slice consisted therefore of a lower, bony, and an upper, fleshy segment. It was divided for microscopic examination through the bony part with great ease with a scalpel.

Microscopic (Plate VI).—The two pieces were fixed in 4% saline formaldehyde, and were completely decalcified almost throughout with Müller's solution. In the lower, bony segment, there is no corticalis. The bone throughout consists of discrete, branching trabeculæ of bone in a relatively abundant fibrous marrow. The fibrous marrow is very uniform and consists of closely packed collagen fibrils, numerous spindle fibroblasts with oval nuclei, and vessels of normal structure. Towards the medullary cavity it encloses a very few, small islands of adipose tissue. Any bony trabeculæ that impinge upon this adipose tissue are surrounded by a zone of fibrous marrow. The trabeculæ are slender throughout the bone, but they are specially slender in the subperiosteal third. In a few trabeculæ towards the medulla there is a small portion of finely fibrillated (lamellar) bone: otherwise the trabeculæ consist of coarse-fibred bone in a single system. Active apposition of bone is shown by numerous osteoid zones, on which the osteoblasts are large and close together. Where the osteoid zones are shown by the shape of the osteoblasts to have been cut strictly at right angles to their surface, they are not deeper than those seen in healing fractures. There are very few osteoclasts in Howship's lacunæ until the upper, fleshy, part of the specimen is approached. Then many are seen in places, particularly in a narrow area immediately beneath the periosteum. In this area spindle fibroblasts are much more numerous in the marrow, groups of lymphocytes infiltrate the marrow, bony trabeculæ are very few and small, and numerous osteoclasts lie upon or near them. Bone is being laid down, however, upon these trabeculæ wherever osteoclasts are absent.

The upper, fleshy, segment is divided by strands of fibrotic marrow into lobular areas of cellular marrow crowded with giant cells. In the cellular areas spindle fibroblasts predominate, but there are many rounded, polygonal and stellate forms. One karyokinetic figure was seen. Collagen and reticulum fibrils are usually scanty. There is a sparse infiltration with lymphocytes, monocytes, and occasional neutrophil leucocytes. Here and there are small groups of cells laden with iron-pigment, and some diffuse impregnation with iron is shown by the Prussian-blue method in the periphery of some lobules. The vessels are capillaries bounded by a single or double row of cells. There are a few small groups of extravasated red corpuscles, and more numerous very small areas of the fibrinoid imbibition that, in association with extravasations, is so conspicuous a feature in most "red tumours." The giant cells resemble osteoclasts. They are very numerous and most are very large. A few are so deeply stained throughout that few of their nuclei can be recognized. Some have one or more large vacuoles in their cytoplasm, several contain an ingested monocyte or neutrophil leucocyte, a few contain a rounded group of red corpuscles. The cellular marrow in the lobules merges into the fibrotic strands which separate the lobules from one another and from the periosteum. In these strands the marrow usually resembles that which predominates in the bony segment, but is more cellular in the greater part of the strand beneath the periosteum. It usually contains trabeculæ of coarse-fibred bone bounded by osteoid tissue. Trabeculæ of osteoid tissue alone are also seen, but comparison of serial sections shows these to be tangentially cut osteoid zones upon calcified cores. The trabeculæ resemble the more slender of those in the bony segment. The osteoid zones appear to be of similar depth. Numerous large osteoblasts lie upon the osteoid zones, but in the more cellular part of the strand beneath the periosteum the zones of osteoblasts are frequently interrupted by osteoclasts in Howship's lacunæ. The lacunæ almost invariably indent osteoid zones and not calcified bone. The junction of the fleshy segment with the bony is sinuous, with concavities towards the bony (plate VI).

Remarks.—The normal architecture has been completely destroyed and all normal bone has been resorbed except a few microscopic pieces near the medulla of the lower, bony, segment. Resorption has, therefore, been very great. There has, however, also been great formation of bone. In the lower segment an incomplete net of delicate trabeculæ of coarse-fibred bone has been formed. In the upper segment similar trabeculæ have been formed in the strands of less cellular fibrous marrow. At the time of operation apposition was in great excess of resorption. Active resorption is confined to the neighbourhood of areas of more active cellular proliferation in the marrow. A conspicuous feature is the occurrence of active apposition by osteoblasts on the trabeculæ which are undergoing active resorption by osteoclasts in Howship's lacunæ. Both apposition and resorption are associated with fibrosis of the marrow. Near the medulla in the lower segment the fibrosis is incomplete, small areas of marrow being still adipose. The trabeculæ that abut upon these areas are, however, bordered by a zone of fibrosis. The portions of old lamellar bone lie in trabeculæ near the medulla. Resorption has, therefore, been less complete here. This agrees with the observation in other specimens that the alterations in the marrow and bone frequently begin and extend from the periosteal surface. In general it can be said that the fibrous marrow is more cellular where conspicuous resorption accompanies apposition than where apposition is alone seen, and there is no bone in the areas of most cellular, least differentiated, fibrous marrow.

The cores of the bony trabeculæ are fully calcified, but the osteoid zones upon them are obviously deeper than in normal healthy bones. The osteoid zones are closely associated with osteoblastic activity. This makes it fantastic to regard them as zones of calcified bone from which the calcium has been absorbed by some chemical process. Their abnormal depth is adequately explained by the exceptional osteoblastic activity. The depth of the zones appears to be within the limits of the zones in healing fractures in healthy adults. There may possibly have been some slight delay in calcification, but there has been no such cessation of calcification as occurs in rickets and osteomalacia.

Formation of bone in the upper segment is confined to septa of fibrous marrow which separate rounded areas of a very cellular marrow rich in osteoclasts. The osteoclasts are not now eroding bone, and they are so numerous, large and evenly distributed that it does not appear justifiable to attribute their presence to recent resorptive activity. The cellular areas have caused expansion of the bone. Histologically they cannot be differentiated from the less anaplastic examples in a series of osteogenetic myelomata, or osteoclastomata, removed from the ends of long bones in skeletons free from general changes. In a nomenclature depending upon morphology, therefore, such areas are entitled to the name osteoclastoma, although their retrogression following excision of enlarged parathyroids points to their not being autonomous neoplasms.— H. M. T.

(2) *Right superior parathyroid body. Macroscopic.*—An oval body, measuring 2·3 by 1·5 by 0·9 cm. and weighing 1·3 grm. (fig. 6.) One surface was convex, the other slightly concave. Externally it was brown-yellow, even, and smooth, except where a cord of areolar tissue was attached near one pole. The cut surface was homogeneous, moist and paler brown-yellow.

The cord of areolar tissue attached it to a mass (2 by 1·2 by 0·6 cm.) which was darker brown and had a slightly nodular surface. The cut surface was a considerably darker brown than that of the oval mass, and glistened conspicuously.

Microscopic.— The oval body is a parathyroid gland. It has a thin capsule of collagenous fibrous tissue, and is divided by a net of delicate collagen fibrils into small acini (Laidlaw's silver method; van Gieson's stain). Many septa contain narrow capillaries, a considerable number contain wide venous capillaries, a few contain veins. Most of the acini are filled with mutually compressed cells, but a few show a central sphere of acidophil, homogeneous coagulum surrounded by a row of cubical cells. There is great variation in the size of the cells and their nuclei. Most of the cells are from ten to fifteen micra in mean diameter with nuclei of from six to seven micra. Amongst larger cells are occasional giants of a mean diameter of twenty to twenty-three micra with a conspicuous nucleus of fifteen micra or more. The nuclei are usually round in the smaller cells and slightly oval in the larger. They contain a close net of delicate threads of chromatin, numerous nodes and one to six acidophil nucleoli in a deeply stained nucleoplasm. The nucleoli are most numerous and largest in the larger cells. In a few cells of medium size the cytoplasm appears granular, and is deeply acidophil (pyronin methyl-green), but usually shows a basophil membrane. In other cells there is a basophil membrane and a basophil reticulum containing a less deeply acidophil substance in its meshes. Other cells have a basophil membrane and a very vesicular basophil reticular cytoplasm; in most cells fragments only of the basophil net are present or vesiculation is complete. In some of the completely vesicular cells a faintly stained acidophil substance is just recognizable. The cubical cells that surround coagulum are almost all basophil and vesicular, but one or two are of the acidophil kind. The predominating picture is of nuclei floating free in a net formed by cell membranes which can only be differentiated with certainty from the periacinar collagenous net by silver impregnation. Occasionally more than one nucleus lies in one of the meshes formed by the cell membranes. By Herxheimer's method a few small spheres in some of the vesicular cells are lightly stained by the scarlet-red. No anisotropic substance was detected with the polariscope. In a portion placed in absolute alcohol as soon as the specimen arrived from the operating theatre and stained by Best's method many of the vesicular cells contain glycogen. The glycogen sometimes is present as small, scattered granules, but usually either fills the cell or forms a crescent in the periphery.

The body attached to the parathyroid consists chiefly of a rounded nodule of slightly fibrotic thyroid tissue. Almost all the acini contain a thin colloid, and are bounded by a row of well-defined flattened cubical cells. A few of these acini are greatly distended with this colloid. A very few small acini are lined with larger ill-defined cells, and appear to be in an early stage of colloid secretion. There are a few groups of lymphocytes, with occasional plasma cells, in lymphatic sinuses. This nodule is separated by a fibrous septum from a strip of thyroid. The strip of thyroid tissue differs in that fibrosis is confined to the neighbourhood of the septum, distention with colloid is not so great, and there is only one minute area of lymphocytic infiltration.

Remarks.—The histological appearances of the parathyroid body suggest a hyperplasia and exceptional functional activity rather than an autonomous neoplasm.

The occurrence of giant cells is often a conspicuous feature in the thyroid of Graves' disease, which cannot be regarded as a true neoplasm.

If the portion of thyroid gland examined can be taken to represent the whole, the gland shows a greater activity than is usual at the age of the patient.—H. M. T.

Progress up to five months after operation.—Twenty-two hours after operation Chvostek sign was positive. On the second day tinglings occurred in the fingers, and the bones were found to be less tender on pressure. On the third day she complained of cramps in the fingers, hands, feet and trunk, so that she felt "tied in knots." On the fourth day, and subsequently, passive movements of the limbs and pressure on the bones caused no pain. Immediately after operation a diet containing milk, ice-cream and eggs was given, together with calcium lactate (5 grm. three times a day). In spite of the high calcium intake, cramps in the limbs persisted, and parathormone (parathyroid extract, Collip) was given by intramuscular injection from the sixth day for twenty-six days (fig. 5). Intramuscular calcium gluconate (10 c.c. of a 10% solution) was used to relieve tetany, and on one occasion intravenous calcium chloride (10 c.c. of a 5% solution) was required (fig. 5). Irradiated ergosterol (one radiostol tablet twice a day) was given over a long period. On the tenth day after operation acuity of hearing became remarkably increased and remained so for five days; subsequently hearing was normal. All manifestations of tetany ceased on the seventeenth day after operation. On the nineteenth day she began to be alert and interested, and found that she could turn over the pages of a book. Five weeks after operation the bony tumour on the dorsum of the right hand had almost disappeared (fig. 3, p. 43), and the swelling inside the mouth, corresponding to the tumour on the mandible, was much smaller. In six weeks, after treatment by massage, she was able to move her arms down to her sides. In eight weeks she was lifted into a chair and soon became accustomed to sit comfortably. Three months after operation normal menstruation occurred for the first time in many years. Muscular development improved, and in five months the weight increased by ten pounds (5 st. 9 lb. 2 oz. on November 24, 1930).

Radiograms: November 24, 1930.—Density of bone shadows, as compared to controls, is not appreciably different from what was seen before operation. Cyst-like areas expanding bone are smaller, especially in the third right metacarpal, and some of them appear to be filling in. Renal calculi unaltered.

Blood-count: November 2, 1930.—Red cells, 4,600,000; Hb., 70%; C.I., 0·85; Leucocytes, 4,400; differential count normal.

Urine: December 2, 1930.—Acid. Sp. gr. 1018. Albumin, faint trace. No sugar. Deposit, amorphous urates.

The average daily output of urine (July-Nov., 1930) was 570 c.c.

CHEMISTRY OF THE BLOOD AFTER OPERATION (FIG. 5).

	Serum calcium (mgm. per 100 c.c.)	Plasma phosphorus (mgm. per 100 c.c.)	Plasma phosphatase (mgm.)
July 3, 1930	10·0	1·5	—
July 7, 1930	7·3	2·0	0·63
July 9, 1930	6·7	2·0	1·06
July 14, 1930	7·3	2·3	—
July 21, 1930	8·9	—	1·06
July 25 1930	11·8	—	1·10
August 7, 1930	10·8	1·8	1·12
August 13, 1930	8·5	2·3	—
August 21, 1930	8·4	2·0	—
September 1, 1930	9·0	2·5	—
September 4, 1930	8·8	2·3	—
September 25, 1930	8·8	2·3	1·08
October 2, 1930	9·3	3·0	0·92
October 13, 1930	9·2	2·0	—
November 3, 1930	9·0	2·3	0·61
November 17, 1930	9·4	2·0	—
December 1, 1930	9·4	2·0	—

CALCIUM EXCHANGE AFTER OPERATION.

Three-day Period	Calculated Intake	Output		
		Fæces	Urine	Total
I	456	330	360	690
II	304	130	420	550

Comment.—In his original description of generalized osteitis fibrosa, von Recklinghausen [1] gives as the diagnosis of two cases: "*Case 5.—Extensive fibrous or deforming osteitis, with tumours and cysts. Case 7.—Osteitis fibrosa, with marked bone softening and multiple osteosarcomata.*" In our subsequent knowledge of this disease there is ample clinical and pathological evidence to establish the benign nature of these giant-celled tumours of bone. The cells themselves are similar to the osteoclasts normally present in Howship's lacunæ. The tumours are, therefore, properly called osteoclastomata.

Gold [2] was the first to demonstrate hyperparathyroidism in a case of generalized osteitis fibrosa, associated with multiple tumours and cysts of bone. Similar cases, in which bone tumours were obvious on clinical examination, have since been recorded [3] [4].

Renal calculi have often been demonstrated in hyperparathyroidism, [3] [5] [6], and renal colic may dominate the clinical picture [7]. The present case, however, shows that persistent slight albuminuria may be the only indication of their presence.

Generalized osteitis fibrosa has sometimes been treated with irradiated ergosterol in the hope of increasing the apposition of bone [8]. In at least one case [9] good evidence has been obtained of the effect of such treatment in increasing the density of bone as judged by radiograms. It is difficult to imagine how this effect is brought about.

Professor Turnbull has shown [10, Case 3] that, although resorption of bone is the predominant feature throughout the skeleton, there is much formation of calcified bone, the formation being actually excessive in focal areas. In the present case, and in two others [10], he has found that where apposition is taking place there is usually exceptional osteoblastic activity, and the osteoid zones are then deeper than in the relatively slow apposition of normal growth in even young children, but these osteoid zones are not deeper than in the exceptionally active apposition of healing fractures in healthy adults. The exceptional depth of the osteoid zones is explained by the exceptional rapidity of apposition, and there is no histological evidence of cessation of calcification. It would seem, therefore, that vitamin D is not required. In the present case no improvement occurred even with the prolonged use of large doses of cod-liver oil, irradiated ergosterol and ultra-violet irradiation.

Decrease in size of osteoclastomata after removal of a parathyroid tumour was first recorded [3] in 1929. Restoration to normal of the menstrual function has also been previously recorded. The temporary occurrence of hyperacusis following the operation is of interest. It has been observed [7] where the serum calcium was low from another cause.

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Addison's Disease Treated by Intravenous Cortical Extract.—S. LEVY SIMPSON, M.D.

Patient, female, aged 51, married. Three children living; one child died from tuberculous meningitis, 1916; one was stillborn. Patient's brother died from pulmonary tuberculosis.

Symptoms date from six months ago, though some general pigmentation followed her last pregnancy (1917), and during the past five years she has had occasional attacks of vomiting.

May, 1930.—Patient began to feel weak and listless; pigmentation became more noticeable.

August, 1930.—Attack of tonsillitis lasting several days; more severe symptoms followed—increasing asthenia, anorexia, nausea, retching and vomiting, apathy and defective memory. Bowels constipated, but occasional attacks of diarrhœa. Abdominal discomfort and some pain in legs. Pigmentation gradually became more intense.

October, 1930.—Further exacerbation of all symptoms, especially vomiting; patient taken to nursing home. Seen by Dr. E. R. Rees and Dr. Stratford Collins. Diagnosis: Addison's disease. Skin and mucous membranes were pigmented. Patient was obviously weak and ill. Pulse rapid and feeble; blood-pressure 94/78.

October 23.—Intravenous administration of glucose solution (2 oz. of 10% solution) was followed by sleep, but 2½ hours later, transitory tonic spasms of whole body occurred. Dried extract of suprarenal gland given by mouth caused no amelioration of symptoms.

November 10.—Dr. Collins communicated with the London Hospital stating that "the patient was very bad and going downhill fast," and that if there was anything to expect from cortical extract "there was not much time to spare." As patient was too ill to be moved to hospital I went to see her at Hollingbourne on November 12. She appeared to be weak and collapsed, paid no attention to our entering the room, replied to questions sluggishly and with a monotonous tone. Speech or slightest movement was obviously an effort. Striking pigmentation of the face and limbs, particularly well marked on dorsum of forearms, back of elbows and finger knuckles. Lower limbs also pigmented, particularly below knee. There was an increase at the usual sites of pigmentation such as axillæ and nipples. There was marked pigmentation of buccal mucous membrane and, to a less extent, of inner margins of lips. Prominent band of pigmentation in waist line. Patient thin but not emaciated. Conjunctivitis (of some weeks' duration) in both eyes. Heart sounds distant, pulse rapid (100) and feeble. Blood-pressure 86/65. No abnormal signs in lungs, abdomen, or central nervous system. Patient was unable to sit up by herself, and on being supported in semi-erect position for examination of lungs, became faint. Temperature subnormal (97° F.). Urine contained faint trace of albumin.

Treatment.—Begun with Swingle and Pfiifner's cortical extract on November 12; intravenous injections of 6 c.c. given twice a day for four days. Marked improvement seen on third day of treatment. General condition was better; vomiting ceased; there were signs of returning appetite; conjunctivitis diminished. Improvement continued during next few days, and when patient was again seen by me on November 19 change for better was extraordinary. She greeted my entry, and was sitting up in bed displaying considerable interest in her surroundings. Her appetite was excellent; she stated that she felt much stronger and wanted to go home soon. The pigmentation had faded. The blood-pressure was not appreciably raised (90/70), but the pulse was moderately strong and heart sounds were more distinct.

Treatment continued on a modified Muirhead régime; 5 m. adrenalin hypodermically twice a day, and desiccated whole suprarenal gland given by mouth. Progress

continued, and when seen on November 30 the patient seemed in good health, her friends stating that she appeared much better than before she fell ill. Blood-pressure was then 110/70.

Dr. B. Barling, who saw the patient in consultation with Dr. Collins on October 23, and visited her out of interest a week after commencement of treatment, kindly sent me the following note:—

> The change was truly remarkable. Whereas one had left a weak prostrated woman, to whom the very effort of speech appeared fatiguing, whose face was pinched, and whose eyes were sunken, one was now greeted by shouts of welcome, long before the door was reached, and was confronted with an almost different being. She was more vigorous, displayed her strength and showed a well-filled face. Her appetite was good and the vomiting had ceased.

Blood-count, November 28, carried out by Dr. Ponder showed "no evidence of primary anæmia." Red-blood corpuscles, appearances normal. Hb. 70%; W.B.C.s, 4,900 per c.mm. *Differential count*: Polys. 50%: lymphos. 38%; hyal. 6%; eosinos. 6% (rather increased).

Comment.—Remarkable though the effect of intravenous cortical extract appeared to be in this case, I should not attempt any conclusions had I not seen similar results in three cases treated with this extract by Dr. L. G. Rowntree at the Mayo Clinic. It is of course recognized that spontaneous remissions occur independently of treatment, but such remissions are usually relative, in that the final state of the patient is not so good as that previous to the exacerbation. I think that probably the cortical extract of Swingle and Pffifner will prove as specific for the crisis of Addison's disease of the suprarenals as insulin has done for diabetic coma. Desiccated suprarenal extract by mouth and (or) adrenalin injections are usually quite impotent in such crises, but they may be of value in maintaining an improved state.

The extract of suprarenal cortex used in this case was an aqueous extract prepared by Swingle and Pffifner. The method of preparation and the successful maintenance of adrenalectomized animals in perfect health is described by Swingle and Pffifner in *Science*, 1930, 1, xxi, 321, 489. The cortical tissue is ground and extracted at room temperature for from twenty-four to forty-eight hours with 95%, and later 85%, alcohol. In the final process the alcohol is removed, and an aqueous solution made up. Sterilization is produced by filtering through a Seitz filter.

[I wish to express my thanks to Drs. Swingle and Pffifner, Dr. L. G. Rowntree, Dr. R. Hutchison, and Dr. S. Collins under whose care the patient remains. I believe this is the first case treated by the above method in this country.]

ADDENDUM.—Radiological examination by Dr. M. Jupe indicated a small calcified area at a point just above the upper pole of the right kidney. This suggested calcification in the suprarenal, but no adequate preparation with castor oil was permitted for fear of exciting diarrhœa. Radiography of the chest was negative. A blood-count (Dr. P. N. Panton) showed: R.B.C.s, 5,300,000; Hb., 70%; C.I., 0·65; W.B.C.s, 8,000; *Differential:* polys., 51·0%; eos., 3%; small lymphos., 25%; large lymphos., 16%; large hyaline, 5%.

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The Question of Immunity in Man to Protozoal Diseases.

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Introduction.—Owing to the immense literature on the subject of immunity in protozoal infections of man and other animals, it is impossible to deal with the matter exhaustively in a short paper. Those interested should consult the comprehensive work by Taliaferro (1929).

Although important observations have been made on immunity of man in protozoal infections, and the varied virulence of strains and species have been studied extensively, it has to be admitted, unfortunately, that little is known of the mechanism of immunity. From a practical point of view no method, at least as far as man is concerned, of satisfactory immunizing against these organisms is known.

Antibodies are formed, but, with few exceptions, specific tests, by which an infection can, with confidence, be detected, are absent. Diagnosis is made either on clinical manifestations, or by finding the parasites. Little is known of the toxins or antitoxins. Knowledge in these respects, perhaps, falls far short of that accumulated in bacteriology. There are several reasons for this, the most important depending on the fact that in protozoal infections of man immune bodies seem either to be unstable or to disappear rapidly from the body after infection has ceased. The inability to obtain and maintain in culture pure strains of parasites free from admixture of blood, serum and other extraneous matter requires further research. Nöller (1917) showed that *Trypanosoma theileri*, *T. melophagium* and flagellates from the gut of insects could be successfully grown on the surface of solid blood-agar plates. This is a great advance in the technique of cultivation. Noguchi (1924) was able to isolate on plates pure cultures of flagellates from the gut of various insects. More recently Mayer and Ray (1928) grew with great success the various species of *Leishmania* on a slightly modified Nöller's medium. The advantage of such surface growths rests on the fact that more or less pure suspensions of these organisms can be obtained by washing the growths off the surface with normal saline. The cultivation of human amœbæ, malarial parasites and the African trypanosomes is, so far, unsatisfactory. The improvement of cultivation methods and the problems associated with immunity present an interesting, important and rich field for investigators.

Four important infections in man will be discussed, namely, malaria, trypanosomiasis, kala-azar and amœbiasis, and an attempt will be made, by leaving out controversial and contradictory observations, to give some idea of the present knowledge regarding immunity in man to these diseases.

Definition of terms. Natural and acquired immunity.—It is proposed to deal with each disease separately, but, before doing so, it may be useful to explain briefly the meaning of the terms used. The resistance of man to a protozoal infection is known as immunity. Immunity may be natural or acquired. Natural immunity is an inherent property in the serum of certain individuals, and is not dependent upon a previous infection. This immunity varies and the nature of the immune substances is unknown.

Man may be completely resistant to an infection with certain organisms—for example, certain species of animal trypanosomes—in spite of the fact that these are being continuously inoculated. For example, under natural circumstances, man is never found infected by *Trypanosoma congolense*, which is extremely pathogenic to

cattle. On the other hand, although man possesses a strong natural immunity against *Trypanosoma brucei* there is good evidence, which will be discussed later, that immunity to this trypanosome, in certain circumstances, may be completely broken down.

Natural immunity may be incomplete or partial, and numerous examples of this condition occur in natural infections of man. In this partial immunity an individual is infected and parasites establish themselves in small numbers in the body, but fail to produce clinical symptoms. This latter type of resistance is common in people who have never before suffered from a previous attack of the invading organisms. Such conditions are often referred to as latent infections and in certain circumstances this type of immunity can be broken down.

Natural immunity varies between extreme limits, as will be well illustrated in malaria. Some individuals are non-susceptible, others moderately susceptible and others very susceptible. A non-susceptible may at any time become susceptible.

Acquired immunity may be produced in various ways and may be active or passive. Active immunity can be brought about by an infection with virulent organisms, followed by recovery, by a milder infection with less virulent parasites, also followed by recovery, by infection with virulent parasites, followed by appropriate treatment, by injection of dead parasites (a vaccine), or by the injection of toxins and the consequent production of antitoxins.

Passive immunity may be accomplished by the injection of antisera or antitoxins. These two last-named methods cannot be considered as of practical use at present in producing an acquired immunity in man to protozoal infections.

Virulence.—Species and strains of organisms vary in their virulence to a very marked degree. For example, trypanosomes of the *T. rhodesiense* type are very virulent to man, whereas *T. gambiense* may cause a very mild infection. This varied virulence depends on several factors, some of which are at present unknown. Virulence can be increased in the laboratory by rapid and numerous inoculations from animal to animal, and it is possible that rapid direct dissemination of an avirulent strain of *T. gambiense*, through the agency of biting flies, may be responsible for the outbreaks of virulent epidemics in certain parts of Africa.

Again, virulence seems to depend upon the time the parasite has been established in a particular host. In ordinary circumstances *T. brucei* is a rare infection in man, owing to the known fact that man is, as a rule, refractory to this trypanosome. If, however, this species becomes established in man the tendency is for the parasite to overrun the unaccustomed host and destroy him. *T. gambiense*, on the other hand, can be regarded as a human parasite, in that it has been established in man for years and under ordinary methods of transmission is of low virulence to human beings, owing to the fact that a certain amount of balance has been established between the host and the parasite.

Varied virulence of the parasite and varied natural resistance of the host react on each other and influence the course of an infection.

Apart from true natural immunity, by which is meant complete resistance to infection, it would seem that by far the most common process is an immunity of a particular type known as tolerance. The mechanism of this tolerance is unknown. An individual who has never before suffered from a disease may have a natural tolerance, as seen in naturally acquired malaria. In a natural tolerance the individual is inoculated successfully and parasites are able to resist destruction but produce no clinical symptoms. Their multiplication is inhibited. Such infections result in *latency* and the so-called prolonged incubation periods which are not uncommon in malaria.

Acquired tolerance is produced by continued infection and reinfection, accompanied by varying symptoms of the disease, over a period of years. A balance is established, finally, which enables the host to live a more or less healthy life while

still harbouring organisms in small numbers. Thus chronic or latent infections exist which produce no clinical signs and give a partial protection against the acute ravages of the disease. Immunity of this type has been extensively studied in protozoal diseases of man and has received numerous names, for example, tolerance, infective immunity, relative immunity, immunity tolerance, partial immunity, labial immunity, and, more recently, premunition (Edm. Sergent, 1929).

Immunity in malaria.—The importance of this disease has led to extensive observations being made on the parasite, the clinical features, the treatment, transmission, prevention and epidemiology. The knowledge of immunity in man is based chiefly on epidemiological and experimental studies.

Natural immunity.—Perhaps natural immunity in malaria might be better regarded as a natural tolerance. It is well known that certain individuals are resistant to infection, or at least to an infection accompanied by clinical symptoms. Such an apparent immunity has been noted amongst certain individuals living in highly endemic areas. The resistance to fever, however, is by no means permanent and is liable to break down, for example, after accidents, operations, or child-birth. This is so well known that experienced physicians in the tropics in charge of patients, especially pregnant women, place them on quinine as a precaution, even in the absence of a previous history of the disease or a negative examination of the blood. It is a matter of very great interest that a woman during pregnancy may show no parasites in the peripheral blood, and no clinical signs of malaria. After the birth of the child, however, in certain of these cases, smears from the maternal surface of the placenta may show massive infections with *P. falciparum.*

Experimental evidence of immunity in malaria.—Recently the use of malaria for therapeutic purposes in general paralysis of the insane has supplied direct proof of the existence of varying degrees of resistance to malaria in persons who have never previously had the disease. Some people are highly susceptible, others relatively resistant and others completely refractory to infections. Yorke and Macfie (1924), Nicole and Steel (1925), S. P. James (1926), Rudolf (1927), and others, have demonstrated very clearly the occurrence of this varied natural resistance. The work of S. P. James (1926) is of particular importance and of great interest. He records that 52 out of 221 patients did not develop the disease after an infective inoculation. A patient never out of England was inoculated on four occasions without production of clinical symptoms. Two patients inoculated on the same day with the same dose showed different incubation periods and varying intensity of attacks. One person subjected to the bites of sixty, eighty, and thirty infected mosquitoes, respectively, on three occasions, may have a relatively light attack of malaria not followed by relapses, whereas another, bitten only once by two or three mosquitoes, may have a severe attack, followed by several sharp relapses. It is important to note that this experimental work was carried out during the treatment of general paralysis of the insane with benign tertian malaria. James reported that many patients intentionally infected may remain free from clinical malaria for a considerable period. After an infective inoculation the patient may escape fever for seven to ten months and then develop acute symptoms of malaria for the first time. Numerous examples of such latent cases are reported in the literature. The writer (1924) in Rhodesia, noted that it was no uncommon event to find asexual forms of *P. falciparum* in the blood of Europeans who were quite unaware that they were infected. Bass, in America, emphasized this state of affairs and reported that about 16 per cent. of persons who gave negative histories of clinical malaria harboured parasites in the peripheral blood.

It would seem, therefore, that complete resistance or absolute immunity to invasion by malarial parasites is a matter of doubt. Resistance to infection varies within wide limits. Individuals possibly seldom escape infection entirely, but may suffer no ill-effects from the presence of the parasites in small numbers. In the

opinion of James this natural tolerance is not due to immune bodies, but to certain chemical conditions of the blood. If the biochemist could solve this problem we should be, possibly, in a position to protect man against the acute manifestations of this disease.

Acquired immunity in malaria.—For years it has been noted that Europeans suffer most acutely from malaria during their first years of residence in hyper-endemic areas, and that afterwards attacks become less severe and less frequent. Daniels (1901) emphasized this feature in Central Africa and compiled the following chart showing the development of immunity in natives as evidenced by the spleen-rate in children and adults.

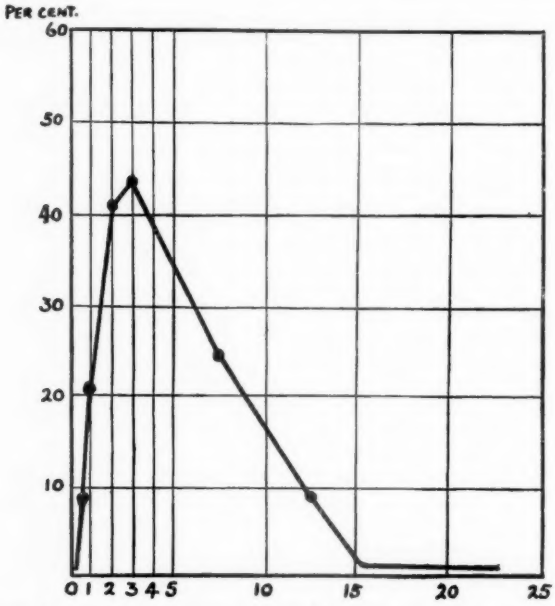

Chart (after Daniels) showing percentage of natives with enlarged spleens (Central Africa). Compiled from the results of the examination of 714 natives under 15 years of age and numerous adults.

The spleen rate is high in children up to the age of 10 years, and falls gradually up to the age of 15, when it is low. This progressive decrease to a low point in adults is a manifestation of the development of immunity or tolerance and, further, the continued high spleen rate in children accompanied by a relatively low rate in adults is a characteristic of hyperendemicity. Such conditions exist where the inoculation of sporozoites is uninterrupted over a long period of years. It is the continuity that is so essential.

Christophers (1924) carried out a series of thorough observations which correlate the parasite rate with the spleen rate. He estimated the endemic index (parasite rate) in children in hyperendemic areas of India and found that infections in children during the first two years of residence were intense and were associated with average parasite counts of about 10,000 parasites per cm. of peripheral blood. He aptly called this the stage of *acute infestation.* Attacks of clinical malaria occurred about once a week, and could be described as almost continuous. The infantile mortality is not known, but must be enormous.

After two years of residence the children who pass through this ordeal of acute infestation show fewer parasites, but the infection rate is still high. Acute attacks occur less frequently, say about once a month. This stage, known as *immune infestation*, lasts through childhood to adult life. In adults there continues to be a high percentage of infected persons, but a low value of infection insufficient, possibly, to produce febrile symptoms. Clinical attacks of malaria occur about once in six months. The peculiar relationship of low value of infection to high percentages of infected individuals is a characteristic of immunity in adults under hyperendemic conditions. The table below by Christophers (1924) demonstrates these facts graphically, and when the results are compared with the chart of Daniels (fig. 1) there is very conclusive epidemiological evidence that tolerance is developed in adults living under hyperendemic conditions.

HISTORY OF MALARIAL INFECTIONS AMONGST THOSE LIVING IN A HYPERENDEMIC AREA. (AFTER CHRISTOPHERS.)

Stage	Age and residence in years	Spleen rate	Per cent. infected	Average No. of parasites per cm. of blood	Frequency of attacks
Acute infestation	0 to 2	88	100	12,526	Almost continuous
Immune infestation	3 to 5	92	96	1,381	Once in 15 days
,, ,,	6 to 10	74	90	818	Once a month
,, ,,	Adults	11	49	121	Once in six months

Christophers found that there was little relationship between the anæmia present in adults and the malarial infection. In other respects there were few clinical symptoms to show that adults were harbourers of the malarial parasite. Gill (1914) pointed out that a spleen rate remaining constant over a period of years signifies a constant immunity, whilst a fluctuating spleen rate implies corresponding oscillations in the degree of immunity possessed by a community. He concluded that in circumstances where perennial infection may occur the collective immunity of a community tends ordinarily to remain fairly constant whilst it is subject to marked fluctuations where transmission of malaria remains in abeyance over prolonged periods.

Where infection is interrupted for a considerable period severe epidemics of fulminant malaria break out from time to time (Gill, 1914). The writer (1924) noted that natives tolerant to malaria while living under hyperendemic conditions quickly lost their immunity by a sojourn in non-malarious areas. This was noticeable when they returned home to the malarious areas. In such circumstances they usually went down with an acute attack of malaria accompanied by the presence of numerous parasites in the peripheral blood-stream.

Active acquired immunity produced by experimental infection with benign tertian malaria.—Soon after the commencement of the therapeutic treatment of general paralysis it was found that some patients who had recovered from an attack were resistant to reinoculation with the same strain. Nicole and Steel (1925) reported such cases, and the work of S. P. James (1926), Rudolf (1927), and others, has shown that such experiences are common. It would seem that persons can be easily immunized against a particular strain of the benign tertian parasite, but that the resistance breaks down if they are inoculated with another species, e.g., quartan, or even with a different strain of the same species.

In bird malaria after a short incubation period of three to ten days and an acute infection lasting about nine days the parasites become so low in number that fever disappears. Whitmore (1918) stated that the canaries developed a chronic latent infection which lasted at least twenty-nine months. During this time the parasites were constantly present in small numbers in the blood-stream, as demonstrated by the successful inoculation of healthy birds. Mazza (1923) found a canary's blood still infective after four years.

Kligler (1930) discusses immunity to reinfection with malaria following treatment and came to the conclusion that in so far as children are concerned no immunity

exists after a cure. Children cured of malaria infection do not possess any increased refractoriness to reinfection, but in an adult group after quinine treatment the rate of reinfection during the same period was much lower, indicating that in the latter there is a heightened resistance to reinfection.

Passive immunity in malaria.—Concerning passive immunity little is known. Sotiriades (1917) investigated the effect of administering immune serum. He injected 10 c.c. of serum, from a case of chronic malaria associated with crescents, subcutaneously into a patient with asexual rings and an enlarged spleen. In eight hours symptoms disappeared. Kauders (1927) administered doses of one to two cubic centimetres of serum from a patient difficult to infect with parasites and this benefited nine out of twelve infected persons. Five of the nine recovered from their fever. These experiments are of interest, but in view of the experimental work of James and others the same results have been attained without treatment since a degree of spontaneous recovery is known to occur frequently in malaria.

Taliaferro and Taliaferro (1929) found that there were no protective or curative substances detectable in the sera of birds which had recovered from acute malaria, and J. W. Scott Macfie in a private communication to the writer confirmed this observation.

Demonstration of immune bodies in vitro.—Attempts of varying success by Thomson (1919), Kingsbury (1927), and Taliaferro, W. H. and L. G. (1927) (1928), have been made to discover a test of practical value for the diagnosis of latent infections. Thomson and Kingsbury obtained deviations of the complement and Taliaferro was able to demonstrate precipitins.

Malaria has been discussed rather fully because it is probable that similar processes of immunity, naturally, with modifications, occur in trypanosomiasis, kala-azar and amœbiasis. These can be dealt with more briefly.

Natural immunity in man against trypanosomiasis.—There is very definite evidence that man is resistant to infection with all species of trypanosomes with the exception of *T. gambiense*. Laveran (1902) first showed that, when normal serum was injected into mice suffering from nagana (*T. brucei*), it exerted a markedly retarding influence on the course of the infection. In a recent paper by Yorke, Adam and Murgatroyd (1930), a most interesting and detailed account is given of the experimental observations on the trypanocidal properties in human serum. Mesnil and Ringenbach (1911) discovered that human serum exercised a trypanocidal action on *T. rhodesiense* in mice. It has been pointed out, however, by Laveran and Mesnil (1904) that the injection of human serum into infected mice causes, as a rule, only a temporary disappearance of the parasites from the blood. It was considered that this trypanocidal action of human serum was absent in vitro, but the recent investigations of Yorke, Adams and Murgatroyd (1929) show that normal human serum rapidly destroys *T. equiperdum*, *T. rhodesiense* and *T. congolense* in vitro at a temperature of 37° C. but that *T. gambiense* is practically unaffected by it. The same authors state that under certain conditions, pathological and dietetic, the trypanocidal substance disappears from the blood of man. If human serum is heated at 64° C. the trypanocidal properties are quickly destroyed and are not restored by the addition of complement.

While normal human serum is, usually, actively trypanocidal it would appear that this property varies in individuals and, further, it has been noted that *T. rhodesiense* may acquire, somewhat rapidly, a degree of resistance to the action of human serum.

Recently Vaucel (1930) has reported an infection of man with *T. brucei* which occurred accidentally in the laboratory. Mesnil (1930) in discussing this accidental laboratory infection refers to the case of Lanfranchi, who was infected while working with a strain of *T. evansi*. As a converse to this state of affairs whereby two persons were susceptible to infection with two strains of trypanosomes not usually

found in man, Mesnil drew attention to the fact that three cases of general paralysis of the insane inoculated with a laboratory strain of *T. gambiense* never showed signs of infection.

In *T. brucei*, the common parasite of animals in Africa, there exists a trypanosome indistinguishable morphologically from *T. rhodesiense*, which, in certain localized areas, is a very virulent parasite in man. Taute and Huber (1919) carried out what might be termed a classical experiment. They inoculated themselves and one hundred and twenty-nine African natives with the blood of animals infected with *T. brucei*. It is stated that no human infections followed, but that control laboratory animals inoculated at the same time developed trypanosomiasis. This experiment is of great value, in that it definitely showed a natural resistance of man to the animal strain of *T. brucei*, but it really failed to prove that *T. brucei* of the cattle and *T. rhodesiense* of man are specifically distinct. The above experimental observations on the trypanocidal properties of normal human serum provide a basis for the explanation of Taute and Huber's results. Yorke and his colleagues (1930) have expressed this clearly, as follows: "The unequivocal demonstration that *T. rhodesiense*, *T. equiperdum* and *T. congolense* are rapidly destroyed in vitro at 37° C. by normal serum or plasma, and that *T. gambiense* is apparently unharmed by either, endorses the well-known phenomenon of the therapeutic action of human serum in experimentally infected mice with an entirely new significance, and seems to us to afford the strongest grounds for believing that man's immunity to infection with the pathogenic trypanosomes of stock and his relative susceptibility to *T. gambiense* are bound up with the property of his serum."

T. brucei of cattle and *T. rhodesiense* and *T. gambiense* of man are probably physiological variations of the same organism modified according to the specific animal hosts in which they have become established (Duke, 1919). Yorke, Adams and Murgatroyd (1930), in summing up their experimental work, suggest that under certain conditions man may lose the protective trypanocidal properties in his blood, and thus may develop an infection with the trypanosome (*T. brucei*) of game. These individuals develop sporadic *T. rhodesiense* infections such as are seen typically in areas where the game is plentiful and there are many *G. morsitans*. The same authors believe that *T. gambiense* infections likewise originated in this manner, but that having occurred in regions associated with the presence of *G. palpalis*, where the contact between man and fly is more intimate than in *G. morsitans* regions, there was a correspondingly greater opportunity for the occurrence of man-to-man infections with the establishment of a strain, race, species, or whatever it may be called, of trypanosomes, somehow attuned to the specific character of the host's serum.

Acquired immunity.—No better example of acquired immunity or tolerance to an animal parasite can be found than in trypanosomiasis. This immunity depends upon continuous inoculation with trypanosomes and a continued low infection. The game animals of Africa, living in constant contact with *Glossina*, have been actively immunized against all the African trypanosomes. How many years it has taken to establish this perfect balance between the host and its parasites is unknown, but it seems fair to assume that within limits the process is comparable to what happens in the natives living in a malarious country under hyperendemic conditions.

Acquired immunity in man against trypanosomiasis, however, is an obscure problem. How far this immunity is influenced by the natural resistance of the host and the varied virulence of the parasites requires further study.

Partial immunity is seen in natives of certain areas in Africa where the only diagnostic feature is chronicity associated with enlarged cervical glands. A partial acquired immunity is also well illustrated after treatment with Bayer 205 and arsenicals. The immunity in this instance is only partial or temporary, since many of these cases relapse after enjoying long periods of fairly good health. In the

experimental treatment of laboratory animals Thomson and Robertson (1926) noted that this partial immunity was a common phenomenon.

Schilling and Schreck (1930) have drawn attention to very important factors which influence the biological qualities of trypanosomes. These organisms may lose their reactivity to serum antibodies and develop into so-called "serum fast" or "relapse strains." Under the influence of treatment they may also develop into "drug fast" strains. If an old laboratory strain of *T. brucei* is passed, however, through the natural transmitting agent, namely, *Glossina morsitans*, a relapse strain changes into an original strain. Any fastness of a relapse strain is an acquired quality which is lost by the passage of the parasite through the insect vector. The practical importance of this is obvious, because if relapse strains passed through the insect unchanged an innumerable variety of strains differing from each other serologically and immunologically would result.

Passive immunity in trypanosomiasis.—Growth-inhibiting antibodies and trypanolysins develop in the blood of animals which have recovered from an acute attack and are suffering from a chronic infection. The sera of such animals have a protective action when injected at the same time as the homologous trypanosomes, but from a practical point of view it is impossible to immunize man or to cure an infection by the therapeutic administration of serum. A protective serum left in contact with trypanosomes for two to four minutes, and the mixture injected into a susceptible animal, produces an inhibition of acute symptoms and prolongs the life of the animal markedly. Within certain limits this action is specific. Taliaferro, W. H., and Taliaferro, L. G. (1922), described immune properties in the sera of rats infected with *T. lewisi*, and further, Taliaferro (1924) and Coventry (1925) described, in rats with the same infection, specific antibodies which inhibit reproduction. Coventry also showed that the sera after a crisis was trypanolytic in vivo. This phenomenon of trypanolysis has been observed in infections with pathogenic trypanosomes and explains the periodic fluctuations in the numbers of parasites circulating in the peripheral blood.

Vaccine treatment.—Little has been accomplished either in producing immunization or cure by the injection of killed trypanosomes (Ross and Thomson, 1911, and Kligler and Weitzman, 1926).

Detection of antibodies in vitro.—As far as diagnosis of human trypanosomiasis is concerned there are no satisfactory serological tests of value. Complement deviation, agglutination, and precipitins have given diverse results. The phenomenon, however, known as *auto-agglutination* of the red cells is frequently of use in the diagnosis of a human infection. Researches on this subject would seem to be necessary in view of the fact that a complement-fixation test is extensively used in America with satisfactory results for the diagnosis of chronic dourine infections in horses (vide Watson (1914) (1915) (1920)).

Natural immunity in leishmaniasis.—Little is known of natural immunity in leishmaniasis from the experimental point of view. Maggiore (1925) subcutaneously inoculated human beings with *Leishmania donovani* taken directly from the bone marrow of a case of kala-azar. No infection was observed. In a second series four individuals were inoculated with *L. donovani* directly from a case of kala-azar, three with cultures of *L. donovani* and three with cultures of *L. tropica*. No infection resulted.

A study of the epidemiology of Indian, Chinese, and Mediterranean kala-azar presents a problem which in the present stage of our knowledge is difficult of solution. In the following tables it is obvious that in India the infants tend to escape infection, and that from 5 years of age to under 30 years the infection rate is high. From 30 years to 50 the rate declines in a marked manner. In Italy, on the other hand, the disease is highest in children and low in adults. A similar state of immunity in adults exists in Northern China.

At first sight these figures might imply that young children possessed a natural immunity to Indian kala-azar and that this resistance is lost with advancing age (and vice versa), and that on the Mediterranean littoral and in Northern China the children were susceptible and adults relatively immune. Adler (1929), however, has suggested that this is best explained by assuming that the transmission in these areas through the agency of sandflies differs in its method. This is an interesting problem requiring further research, and it is a matter of interest that children in Italy with visceral leishmaniasis seem to resist malarial infection.

McCombie Young (1924). Distribution of Kala-azar in India according to Age.

	Under 1 year	1 to 5 years	5 to 10 years	10 to 15 years	15 to 20 years	20 to 30 years	30 to 40 years	40 to 50 years	Over 50 yrs.
No. of cases	11	1,520	3,528	3,390	2,834	2,995	1,607	529	24
Percentage of cases	0·06	8·59	20·5	20·2	16	16·9	9·6	2·9	0·37

Peradiso's Data (1926). Italy.

	1 to 6 months	6 months to 1 year	1 to 2 years	2 to 3 years	3 to 4 years	4 to 5 years	5 to 10 years	10 to 15 years	Not stated
No. of cases... ...	21	168	694	248	116	46	46	7	78
Percentage	1·47	11·8	48·74	17·42	8·15	3·23	3·23	0·49	5·48

Kala-azar can exist in man in a mild form with little or no clinical symptoms. Napier and Das Gupta (1930) in an analysis of cases of post-kala-azar dermal leishmaniasis in persons of all ages, found that the majority gave a history of having suffered from the disease and had received treatment. Others had suffered from fever and splenic enlargement, but a few gave no history of any such illness. The latter (i.e., the cases below the clinical threshold) bring this disease in line with those mild forms seen in other protozoal diseases.

Acquired immunity in kala-azar.—Cases which recover spontaneously or through treatment develop a tolerance to the acute disease associated with the presence of the parasite. This is proved by the observations of Napier and Das Gupta mentioned above. Brahmachari (1922) first drew attention to what he termed dermal leishmanoids in patients after antimony treatment. Acton and Napier (1927) recorded further examples. That these skin conditions are much commoner than was previously suspected is obvious from the work of Napier and Das Gupta, who have collected and studied about 150 cases during a period of about two and a half years. The dermal lesions make their appearance from one to two years after all signs of the visceral infections have disappeared. The skin condition does not seem to develop during the visceral stage, but in three instances the visceral lesions reappeared when the dermal conditions developed.

The period which elapsed between the conclusion of treatment for kala-azar and the first signs of the skin condition varied from less than one year to six years. Most cases occurred in adults between the ages of 20 and 30 years of age.

The epidemiology of both Indian and Mediterranean kala-azar, as seen in the tables of McCombie Young (1924) and Paradiso (1926), indicate that there is a gradual development of immunity established by previous infection. How many mild cases of kala-azar exist in endemic areas is unknown, but it is quite possible that they are much commoner than was previously suspected; they may be overlooked because the infection is mild.

Nicolle and his collaborators have shown that a first attack of visceral leishmaniasis produced immunity in dogs and monkeys, if the cure was complete and of several months' duration. A dog cured of kala-azar was immune to oriental sore, but a monkey cured of oriental sore was only partially immune to kala-azar.

There is some information concerning natural immunity or resistance to infection with oriental sore. Adler inoculated two people from a sore, and in one individual the lesion failed to develop.

An active acquired immunity has been recognized for many years in Mesopotamia, where it was a common practice to inoculate children deliberately on some unexposed part of the body to prevent the disfiguring sores on the face. Immunity has been recorded in dogs after cure, but it would seem that a previous infection does not always confer complete immunity. According to Marzinowsky and Schourenkoff (1924), an experimental sore only produces immunity when allowed to run its full course. Adler, in a personal communication, has informed the writer that, after the natural cure of an experimental sore on his own arm, he completely failed to infect himself with the same strain and another biologically different to the first.

Passive immunity.—Attempts to treat kala-azar and oriental sore with vaccines have not been carried out extensively. Jessner and Amster (1925) drew attention to a definite skin reaction which followed the injection of a vaccine of *Leishmania tropica* subcutaneously into a man and a dog during and after recovery from an oriental sore. These authors directed attention to the possibility of employing vaccines for the purpose of immunizing against infections. Attempts, however, to treat oriental sore by vaccines have given more or less indefinite results (Parrot, Donatien and Lestoquard, 1927), but Row (1912) believed that a vaccine of *L. tropica* was helpful in hastening a cure of oriental sore. More recently Dr. J. C. Ray undoubtedly hastened a clinical cure in two cases of chronic sores in Indians by the subcutaneous injection of killed cultures of *L. tropica*. These observations have not yet been published, but the writer and others were impressed by the rapid improvement following the treatment.

As regards kala-azar there is little definite information, and attempts to treat with vaccine seem to have been unsatisfactory. Killed cultures were used by Longo (1912) in two cases and by di Cristina and Caronia (1912) in seven cases.

Diagnosis of leishmaniasis by skin reaction.—Wagener (1923), by using an alkaline extract of *Leishmania tropica* bodies, obtained a very definite skin reaction in oriental sore infections, and Montenegro (1926) confirmed this observation, but found that the reaction was not specific in cases of *L. tropica* and *L. braziliensis*. Ray (1928), however, prepared various types of antigen from cultures of *Leishmania donovani* and *L. tropica*, and obtained clear-cut positive skin reactions, which he stated were specific in rabbits immunized by vaccines of *L. donovani* and *L. tropica* respectively.

Laboratory diagnosis of kala-azar.—The only certain means of diagnosis in kala-azar seems to rest on the findings of parasites, but various methods, such as the aldehyde, serum globulin and antimony tests, have given promise of some help. Noguchi (1924) introduced agglutination methods to distinguish species, and concluded that *L. donovani* and *L. infantum* cross agglutinated and could be distinguished from *L. tropica* and *L. braziliensis*. Kligler (1926) confirmed this observation. Adler and Theodor (1929), however, carried out investigations on the same lines and pointed out that the problem of agglutination was a very complicated one, especially because strains may be auto-agglutinable. These workers could not convince themselves that *Leishmania* species can be thus differentiated with certainty. Wagener and Koch (1926) found group agglutinins in *L. tropica*, *L. braziliensis* and *L. donovani* (China). J. C. Ray (1929) points out that it is necessary to obtain high titre sera in order to cut out the cross agglutination phenomena.

Complement-fixation in kala-azar.—At present this method of diagnosis can only be considered to be in the experimental stages. Hindle, Hu and Patton (1926), however, obtained well-marked complement-fixation in nineteen cases and partial results in five, in twenty-four cases of kala-azar diagnosed by liver puncture.

Amœbiasis. Natural immunity.—The only experimental evidence of immunity in man to *Entamœba histolytica* is that supplied by Walker and Sellards (1913). Twenty men were fed on *E. histolytica*. Both cysts and free forms of this amœba

were used. Eighteen out of the twenty acquired infections, but four only developed acute symptoms of dysentery after incubation periods of 20, 57, 87 and 95 days respectively. Fourteen became carriers of the cysts, and two never showed evidence of infection. Such results show that man may be resistant, or susceptible to infection, and, further, those individuals who showed cysts only prove that man may develop a tolerance to the parasite. Such tolerance might, of course, in certain circumstances be broken down. Another interesting experiment is described by Walker and Sellards (1913). An individual received cysts from a convalescent carrier who had previously suffered from acute amœbic dysentery, and he became a contact carrier (i.e., a cyst carrier who showed no acute symptoms). A third man received cysts from the latter and he also became a carrier only. A fourth individual who received cysts from the third developed acute amœbic dysentery.

Recent work by Cleveland and Saunders (1930) on the virulence of *E. histolytica* is of very great interest. By experimental inoculation of cultures of *E. histolytica* into the liver and intestine of kittens it would seem that an increase in virulence was produced by passage. Evidence, however, pointed to this increase of virulence being due to increased virulence of the accompanying bacteria rather than the amœbæ. Further, the experimental evidence of Cleveland and Saunders indicates that the amœbæ alone do not produce a liver abscess in kittens unless accompanied by certain pathogenic bacilli.

These observations open up an entirely new line of research, as it is possible that the pathogenicity or non-pathogenicity of a strain of *E. histolytica* may depend to a certain extent on the accompanying bacterial flora in the intestine. The presence or absence of certain bacteria in the intestine may determine whether a person is resistant to infection, or susceptible to acute dysentery. Such factors might explain also the presence of healthy carriers of the pathogenic cysts.

Acquired immunity.—This form of immunity is again of the type common to those other diseases already discussed, in which there is a low type of infectivity unassociated with clinical dysentery. This resistance seems to be more complete in some persons than in others and, as in other conditions, is liable to break down. The so-called tolerance to *E. histolytica* as manifested by numerous convalescent and contact carriers is a problem of extreme interest. Are the minute tissue lesions in carriers so small as to defy detection by pathologists, or is the parasite capable of becoming a harmless commensal feeding on the bacterial content of the intestine? If the latter condition is possible it is a remarkable example of a pathogenic tissue invader becoming a harmless inhabitant of the lumen of the intestine, and a perfect example of balance established between the host and its parasite.

Hegner (1927) in an interesting book on host-parasite relations between man and intestinal protozoa showed that an analysis of *E. histolytica* infections of Chinese and foreigners gave evidence that a certain amount of acquired tolerance to acute manifestations of amœbiasis was developed in Chinese. Foreigners exhibited both more severe and more mild symptoms than Chinese and were correspondingly low in the number of healthy carriers when compared with the Chinese.

Hegner concluded that the data available indicated that although the Chinese are more highly infected their infections are not so severe as those of foreigners and that, therefore, a real difference existed in susceptibility and resistance of the different races to *E. histolytica*.

Serology of E. histolytica infections.—Positive complement-fixation tests have been obtained by Izar (1914) and Craig (1927) (1928), and Wagener (1924) obtained a specific precipitin reaction. So far, however, no test of practical value has been obtained.

Conclusions.—(1) In the four protozoal diseases of man briefly discussed, namely, malaria, trypanosomiasis, kala-azar and amœbiasis, there is definite evidence of a natural resistance to infection. Some individuals may be completely refractory to an infection, but the most common type of immunity seems to be a natural tolerance associated with the presence of parasites in small numbers.

(2) This resistance or natural tolerance may from various causes be completely broken down. The first acute manifestations of an infection often date from some cause which lowers the general body resistance.

(3) A definite acquired immunity or more correctly an acquired tolerance depending on the presence of parasites in small numbers can be brought about by continuous and repeated infections as is well illustrated in malaria and trypanosomiasis and to a less extent in leishmaniasis and amœbiasis. Again, this acquired immunity can be easily broken down if reinfection is interrupted for a considerable period. Any debilitating cause may also bring about loss of resistance.

(4) Little is known of the characters of natural or acquired immune bodies. Natural immunity depends upon some unknown properties in the normal serum, and from recent observations of Yorke, Adams and Murgatroyd would seem to be dependant on such factors as diet. These immune substances become less or disappear from the serum in certain pathological conditions of the body.

(5) In acquired immunity, on the other hand, antibodies of an unknown nature seem undoubtedly to be formed, but these are either unstable or quickly eliminated from the body after complete disappearance of the parasites. In other words, this acquired immunity seems to depend to a large extent on the continued presence of a low infection with parasites. It seems further, to depend upon more or less continued inoculation with fresh strains of parasites and if this continued inoculation is interrupted for a considerable period the immunity is broken down. Any debilitating cause can also bring about loss of resistance.

(6) Practical methods of passively immunizing man are at present of little value. The use of vaccines or antisera in treatment requires further observations.

(7) It would seem, however, that the important observations already made on natural resistance and acquired immunity to these infections open up a hopeful field to research workers, because, if one could find the factors or biochemical properties influencing refractoriness to infection, it might be possible to protect individuals either completely from infection or from the ravages of acute infestation.

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Discussion.—Dr. P. MANSON-BAHR said that he was at a disadvantage in discussing protozoal immunity in comparison to bacterial, in so far as the protozoa varied within wide limits in virulence and in the natural resistance of the host. The latter was a factor to which too little attention had been paid. There appeared to be a natural immunity to malaria in certain individuals. Everyone with tropical experience could cite instances of men living in highly malarious districts and remaining free from the disease. During the late war, infections with the subtertian parasite were found in men in apparently good health. There were instances,

too, of great tolerance to trypanosome infections, and he (the speaker) had recently treated a case of *T. gambiense* infection in a man who showed no clinical signs of the disease until he had left Africa for over a year. Examples of spontaneous cure from kala-azar were also known. With regard to amœbiasis, we were at a distinct disadvantage, because failure to infect *per os* was no criterion of resistance; rather, he thought, an endeavour to infect volunteers should be made by the injection of infectious material per rectum.

Col. S. P. JAMES said: Professor Thomson has referred to the experiments on acquired immunity which we have been able to make in connection with malarial therapy at the Horton Mental Hospital, Epsom. I should be sorry if it were thought that we are prepared to generalize too widely from those results. They are true for the individual cases concerned, but one of the most puzzling findings in experiments on immunity to malaria, as well as in other aspects of the disease, is that the same experiment gives different results with different individuals. In a paper read at the Royal Society of Tropical Medicine, in 1926, I distinguished between people who are abnormally susceptible to malaria and people who are abnormally refractory, and noted the intermediate class to which most people belong, namely, the class of people of "normal" susceptibility. In experiments on immunity some such classification as that also seems to be necessary in order to explain the apparently contradictory results of test experiments and in order to correlate results with the well-known clinical and parasitological observations indicating that in severely endemic areas in the tropics the indigenous inhabitants acquire an immunity only after repeated infections and reinfections during several years. Other difficulties in studying the subject are: (1) That malaria caused by direct blood inoculation is a different disease from malaria caused by mosquito bites; (2) that in experimental work, account must be taken not only of different species of parasites, but of different strains of the same species; (3) that the different species seem to be mutually antagonistic when in the human host; (4) that acquired immunity does not occur as a rule until the primary infection has been allowed to run its course for some time and has been followed by a long-interval recurrence ending in spontaneous recovery. In about half our patients a single primary attack does not suffice to make patients refractory, but patients whose attack is followed seven or eight months later by a recurrence ending with spontaneous recovery, usually become quite immune thereafter. One of our patients in this category was infected by mosquito bites on January 31, 1926. Her attack lasted nineteen days. She had no relapse until nine months later when she had a recurrence lasting three days followed by a recrudescence lasting one day. Ever since, she has been completely refractory to infection by mosquito bites and by blood inoculation with the same strain, as proved by repeated trials in January and July, 1928, June and November, 1929, and September, 1930.

Professor R. T. LEIPER, speaking from the metazoal aspect, said that failure of experimental inoculations should not be taken as indicative of natural immunity. The subcutaneous injection of water containing bilharzia cercariæ seldom resulted in infection of experimental animals which were highly susceptible to infection by immersion.

Helminth investigations suggested that failure of infection resulted not merely from the presence of antagonistic material in a host, but from the absence of certain necessary energizing substances, e.g., some growth-promoting substances, which were essential to enable the helminths to pass through the metamorphoses necessary before adult stage was reached, and it might even be that the successful action of certain drugs was due to their effect in inhibiting or fixing those vital substances in the host.

Dr. HUGH STANNUS said he was of opinion that there was no such thing as absolute natural immunity to malaria. Could one reconcile the 100% infection rate in native children in hyperendemic areas with the attack rate of 83% induced in paralytics, quoted by Colonel James. He suggested there were factors determining the failure to infect which required investigation. He very much doubted the actual truth of the statements quoted by Dr. Manson-Bahr regarding the immunity of Livingstone and Emin Pasha. He believed they were cases of acquired immunity. The question had a very important bearing on the treatment of malaria, and he suggested that the evidence supported a line of treatment consisting in allowing the fever of the first attack of malaria to run some few days before commencing the exhibition of quinine. Full doses should then be given for some short period with similar treatment for any relapse. In this way immunity might be established.[1]

[1] It is interesting to note that in malaria we have a disease in which, as far as is known, the parasites remain within the blood-vessels, whereas immune bodies are produced by various tissues of the body and are so to speak secreted into the blood-plasma. Might it not be possible to induce an artificial immunity by introducing the parasites into the tissue?

Section of Dermatology.

[*December* 18, 1930.]

Two Cases of Congenital Ichthyosiform Erythrodermia.—H. W. BARBER, M.B.

At the meeting on June 19, 1930, I showed a girl, aged 4, with this condition.[1] In that case the entire skin had been affected at birth. But as the patient grew older certain parts had became normal, and these parts corresponded strikingly to those exposed to light. I am now showing two sisters with the same condition, and in both the distribution is more or less identical with that in my previous case. The older girl is aged 14 years, the younger 7 years. There is no family history of the complaint, to the mother's knowledge. In both sisters the erythrodermia was present at birth, but was not generalized, as in my earlier case, the distribution having been much the same as now, except that the face, hands, and elbow were not involved until later. Therefore it is unlikely, at any rate in these cases, that exposure to light and air has anything to do with the distribution, and I was probably wrong in suggesting that in connection with my first case. It is striking how abruptly the erythrodermia ends on the upper part of the thighs in the younger child, and above the eyebrows, and that was seen in my earlier case.

Psoriasis Arthropathica.—H. W. BARBER, M.B.

S. M., aged 31, this is a characteristic case of psoriasis arthropathica. The psoriasis began on the scalp and forehead about five years ago; the arthritis is only of a few months' duration.

Present condition.—There is severe and widespread psoriasis; in parts the appearances resemble those of an exfoliative dermatitis, to which these arthropathic cases seem peculiarly liable. The arthritis chiefly affects wrists, finger-joints, elbows, and knees. From time to time there is a slight evening temperature, and the patient is subject to sweatings.

Investigations.—No source of focal sepsis of any moment has been discovered. Radiograms of teeth normal (Mr. Worth). Cultivation of fæces gave growth of *B. coli* only. Dr. Eyre kindly saw the case for me, from the point of view of an underlying infective cause, and found nothing of significance.

Urine.

Date	Time	Vol. oz.	Free acid	NH3	Urea percentage	Urates	Urobilin
Dec. 5	3 p.m.	6	1·0	2·3	3·09	+	+
,, 6	4 p.m.	12	Nert.	1·6	3·91	+	+
,, 6	5 a.m.	2	1·5	3·2	2·67	+	+
,, 6	7 a.m.	6	0·5	1·8	2·54	+	+

Blood-sugar.—170 mgm. per 100 c.c.; *amino-acid*, 5·6 mgm. per 100 c.c. *Van den Bergh* reaction, negative.

I agree with Garrod and Evans that psoriasis arthropathica (or, as they call it, "arthropathia psoriatica") is a definite clinical entity, that the psoriasis and the arthritis are intimately connected, and probably due to a common cause, and that the arthritis presents features that distinguish it from the so-called infective type of rheumatoid arthritis.

1 *Proc. Roy. Soc. Med.*, 1930, xxii, 1636 (Sect. Derm. 70).

Discussion.—Dr. G. B. DOWLING asked whether any Member knew of a case in which the arthritis had preceded the psoriasis. The usual history was that the psoriasis was of an intractable type, and grew worse in the course of years: then at a late stage the arthritis supervened. He had not seen a case in which arthritis had appeared first.

Dr. RIPLEY ODDIE said that the only case of this kind that he had seen was one in which the psoriasis began at 25 years of age. The patient was seen at hospital when, at the age of 41, she had her first attack of arthritis. The description given by Dr. Barber fitted that case well. The patient had had attacks of psoriasis lasting three or four weeks, almost yearly, and in the intervals was quite free.

The PRESIDENT said that two cases of psoriasis and arthritis had recently come under his notice.

In the first, that of a woman under the charge of Dr. Cassidy, at St. Thomas's Hospital, two severe attacks of arthritis and psoriasis had occurred contemporaneously, but there was a history of previous psoriasis without arthritis. In that case the psoriasis was of the exfoliative dermatitis type, with large abundant scales. He (the President) thought this was the usual type occurring with arthritis.

In the second case, all the nails were affected by a condition resembling psoriasis, but there were no lesions on the body, and no history of previous attacks affecting the skin. There was marked bulbous swelling of all the terminal phalangeal joints of the fingers, and a radiogram showed definite absorption of the bones.

Dr. H. C. SEMON suggested that Dr. Barber should ask Professor Eyre to investigate the patient's fæces from the point of view of late lactose fermenters in these cases. Dr. E. Bach had investigated one such case for him (the speaker), and made a vaccine which had a very prompt effect. The patient felt ill after the injection, but in a few weeks the eruption had cleared up, and the rheumatic trouble—which was not so definitely arthritic as in the present case—also involuted. He (Dr. Semon) had often wondered whether the eruption and the arthritic changes were both dependent on some abnormal intestinal organism in this type of psoriasis.

Dr. W. J. O'DONOVAN said that the clinical consideration of an arthritic form of psoriasis might be properly extended over a far wider field than was here suggested. The rheumatic association was often familial. He had seen a mother with coincident psoriasis and rheumatism bring into his room two daughters, one with rheumatism only, and another with psoriasis only. The term "rheumatic" had a wide implication, being applicable to patients who complained for years of joint pains without notable change. "Rheumatism" included fibrositis of many types, the peri-articular form, and arthritis deformans. Some dermatologists looked upon gonorrheal keratodermia as an instance of the association of psoriatic skin changes with contemporary acute arthritis. He was certain that in many cases rheumatic symptoms could precede psoriasis for many years, but the reverse was equally true. He was certain also that cases of severe arthritis with psoriasis were not all of one type. In Dr. Barber's case shown to-day there was peri-articular rheumatism, but he (Dr. O'Donovan) had also seen a middle-aged Jewess with gross rupial psoriasis, and subluxation of the knee-joints. Acute tonsillitis, and acute arthritis, with an outcrop of psoriasis in the same attack of illness, further extended this clinical picture.

Dr. F. PARKES WEBER suggested that in the case mentioned by Dr. Semon, as a strong reaction followed injection, the improvement might have been a non-specific result. There probably were present those who would remember the days when every large hospital had a few severe cases of typhoid fever, and it was known at that time that a patient who had psoriasis before the typhoid fever, sometimes left the hospital without psoriasis. The freedom from psoriasis in such cases lasted a variable time. A similar temporary disappearance of psoriasis sometimes followed other severe infectious diseases.

Dr. SEMON, in reply to Dr. Parkes Weber, said that the patient felt ill but there was no anaphylactic shock following the injection. If typhoid fever had the effect of getting rid of the psoriasis it might have been an indirect effect by way of altering the intestinal flora.

Dr. H. MACCORMAC said he was convinced that a definite relationship existed between psoriasis and one form of arthritis. He did not think, however, that it was necessary to attribute the joint condition to an infection. In most cases the arthritis was associated with

a severe or an acute variety of psoriasis, and he suggested that the arthritis might be a result of the absorption of some toxic substance from the severely disordered skin. One need not seek far for a parallel. Dermatologists were familiar with the non-infective arthritis following the intramuscular injection of bismuth for syphilis, in which the joint changes were presumably due to the absorption of a toxic substance introduced from without.

The PRESIDENT said it was not uncommon in his experience to get a history of some acute febrile condition, such as scarlatina or tonsillitis, immediately preceding a first outbreak of psoriasis.

Dr. BARBER, in reply, said that he had had one characteristic case, in which the arthritis had preceded the psoriasis. The patient had had rheumatoid arthritis of this type since her early twenties, but her psoriasis appeared much later in life. He agreed with the President that it was in these arthritic cases one saw the most extensive exfoliation. Often such cases developed a general exfoliative dermatitis.

In answer to Dr. Semon, he thought it likely that the antigen, to which the arthritis and the psoriasis were due, was probably absorbed from the gut. In favour of this view, perhaps, was that one found evidence of hepatic insufficiency, suggesting that the liver was being damaged by some toxin. But the effect of giving a vaccine of late lactose fermenting coliform organisms could be explained as being due to protein shock. These organisms were very toxic, and vaccines made from them produced severe reactions.

One could recognize at least two types of psoriasis. There was the type met with in fair-complexioned people, which began as a rule in childhood, and might precede or follow ordinary typical rheumatic fever of children. Like this disease the psoriasis frequently followed tonsillitis, the patient having an acute outbreak of psoriasis with each succeeding attack of tonsillitis. There was another type in which the psoriasis began in adult life, and had no connection with tonsillitis or focal sepsis, but might be complicated by an arthritis of the non-infective type.

He also agreed with Dr. O'Donovan that, if one took family histories of patients with psoriasis, one frequently found that other members of the family were affected or had rheumatoid symptoms, such as arthritis, lumbago or sciatica. When a woman with psoriasis arthropathica was pregnant, her symptoms might entirely disappear, yet within a month of the birth of her child they were likely to return with increased severity.

Loa-Loa.—R. T. BRAIN, M.D.

D. L., a single woman, aged 29, attended Dr. O'Donovan's clinic at the London Hospital on December 17, and gave the following history. Fifteen months ago she went to the coastal area of Nigeria as a missionary. She remained in good health and entirely free from skin trouble until six weeks ago, when a dome-shaped, red swelling, three inches in diameter, and raised about a quarter of an inch, appeared on the left forearm. The swelling was rather tender, but not irritating, and disappeared spontaneously in four days, leaving no trace. Three weeks ago, whilst on the boat returning to this country she noticed in a mirror a white worm about one inch long moving in the skin of the cheek towards the inner canthus of the left eye. There being no doctor on board she was advised by an experienced passenger to apply pressure to prevent the worm from entering the eye, and when she did so the worm retreated and disappeared. Apart from slight irritation, no local disagreeable sensations were felt during the incident. A week later a painful inflammatory swelling formed in the scalp one inch behind the left ear and broke down, discharging a central core like a boil, and leaving an ulcer with indurated edges. Ulcers of this type are known to occur in loa-loa, and it is believed that the inflammatory reaction is caused by a dead worm. Examination of the ulcer revealed nothing specific. A blood-film (December 17, 1930) showed an excess of eosinophils but no parasites. The Wassermann reaction was positive. It is doubtful what value can be placed upon this test because there was no clinical evidence supporting a diagnosis of syphilis, and it is known that positive reactions occur in non-syphilitic patients suffering from certain tropical diseases, notably yaws.

ADDENDUM.—The post-auricular ulcer demonstrated at the meeting had healed when the patient was seen later (January 1, 1923), after local X-ray therapy: no anti-syphilitic treatment had been tried.

A good account of loa-loa is given in Manson's "Tropical Diseases," from which the following brief summary is extracted:—

Loa-loa has been known for over three hundred years and is probably of West African origin. It was first described by Guyot in 1778, and in 1891 Manson found a new species of micro-filaria in the blood of two negroes, in one of whom a worm had crossed the eyeball. This newly discovered parasite showed slight morphological differences from *Filaria bancrofti*, and it was only found in the blood during the daytime, so Manson called it *Filaria diurna*. The mangrove fly was suspected of carrying the larval form of the parasite, and after infection of the human subject development was very slow, and adult worms might not appear for from three to five years. In some recorded cases worms have been found 4 to 5 cm. in length and 0·5 mm. thick. They can move 2 to 3 cm. per minute in the loose subcutaneous tissues, and occasionally they cross the ball of the eye.

It was supposed that the adult worms moved about until fertilization was accomplished, and then the female found a site near a blood-vessel where she deposited ova so that the young filariæ could enter the blood-stream. Worms have been seen at intervals in a single host for fifteen years.

The other peculiar feature of loa-loa is the appearance of Calabar swellings, which arise as painless tumours oval or round, up to 8 cm. in diameter, somewhat inflamed, not pitting on pressure and usually disappearing spontaneously in three or four days.

The swelling which appeared on D. L.'s arm was obviously of this type.

Dr. WHITTLE said that five months ago he had seen, in consultation with Dr. Nourse, of Cambridge, a case of the kind in an undergraduate. The patient had a temperature and some ambiguous signs in the chest, and his doctor thought he had an attack of malaria, but a blood-film was negative. Three weeks later swellings developed in the skin ("Calabar swellings") which were not recognized as such at the time; they were on the forearm, upper arm, back and forehead. By that time angio-neurotic œdema had been considered as a diagnosis. A blood-count showed eosinophilia 45%, and that put one on to the right track. He was asked by the doctor whether he would like to see a worm crossing the conjunctiva, and an ophthalmic surgeon also attended, but the worm escaped as soon as the surgeon applied his preparation to the eye. In the evening it was said to have appeared in the lid, and, when a surgical needle was put into the skin, it put its head out, and was withdrawn with forceps. The patient had returned from Nigeria six months before. There had been no previous history.

Schamberg's Disease.—W. N. GOLDSMITH, M.D.

H. H., female, aged 16.

History.—The rash was first noticed on the legs in February, 1930, and it has gradually become worse. From the beginning it consisted, according to the patient, of a brownish-yellow discoloration, which has hardly altered in tint. There have never been any subjective sensations. I first saw the patient in September, 1930, with a sheet-like discoloration, mainly on the inner aspect of the thighs, and some red points, which at first I took to be purpura and telangiectases. She was admitted to hospital for investigation. Careful examination revealed that the main eruption extended to the buttocks and hips and that early stages of the disorder were present on the arms and the scapular region, where it consisted almost exclusively of reddish-brown cayenne-pepper dots. While under observation a number of new specks became visible, but the main eruption showed absolutely no change in colour. The appearances and evolution tallied exactly with Schamberg's description.

There is some acrocyanosis. General examination revealed nothing abnormal, except that over a period of a month the temperature was always raised in the evening, generally to 99°, but quite often to between 100° and 101°. No explanation of this was found. A skiagram of the lungs was normal, and a tuberculin skin

test was negative. Blood and urine were normal morphologically and sterile. The Wassermann reaction was negative.

Biopsy.—A portion of skin was taken from the most deeply-pigmented part of the right thigh. The specimen was kindly examined for me by Mr. W. G. Barnard, who reports as follows:—

"There is a patchy chronic inflammatory infiltration immediately beneath the epithelium. The cells taking part in the reaction are lymphocytes, plasma cells, histiocytes and a few fibroblasts. There is no obvious pigment either in the epithelium or sub-epithelial tissues. In the inflamed areas there is a fine granular pale pinkish-brown substance lying free in the tissue spaces. This substance does not give an iron or a melanin stain. The sub-epithelial fibrous tissue appears to be increased slightly and to be more hyaline than normal."

Comment.—It is still stated in most modern textbooks that Schamberg's disease is confined to males. It is certainly exceedingly rare in females, but one or two other cases have been reported. The disease is often confused with Majocchi's purpura telangiectodes. But many authorities, without in any way confusing the two, hold that they are essentially the same disease in different degrees of intensity, that is to say, that they are primarily hæmorrhagic diatheses. Clinically Schamberg's disease is distinguished not only by the absence of ring formation or atrophy, but also by the absence of purpura in the ordinary sense of the term. But Kingery and several more recent investigators have shown the presence, histologically, of iron-containing blood-pigment. This is generally not present in great amount, and though the blood-vessels show mild inflammation of their coats, there has never been observed any rupture or extensive extravasation. They conclude that the red blood-cells escape by diapedesis, disintegrate, and leave behind granules of hæmosiderin. But all biopsies have shown the presence of quite a high degree of papillary and sub-papillary inflammatory infiltration. This would be quite enough to explain the presence, in some cases, of small quantities of blood-pigment, particularly if specially looked for. On the other hand, this very slight diapedesis of red cells, which is not even always observed, would not be enough to explain the inflammation. It rather appears to me therefore that the disease is primarily inflammatory and not hæmorrhagic. In my sections no pigment is seen, but there is well-marked evidence of inflammation. The cause of the discoloration is therefore obscure. Possibly this mild inflammation over such a large area of the skin surface is enough to account for the rises in temperature.

Discussion.—Dr. H. W. BARBER said that he had recently had a private patient with the most extensive eruption of Schamberg's disease that he had ever seen. The patient was an elderly man, with normal blood-pressure, and with a moderately good heart for his age. The condition began on the leg, and, when seen by the speaker, was extensive on the legs and arms, with a little on the back. A month later some of the patches on the legs were much paler, and an acute outbreak had developed on the back, some of the previous lesions having faded. The outbreak was associated with intense itching. The patient was subject to recurrent sore throat, for which he was being given an autogenous vaccine of a hæmolytic streptococcus; the acute outbreak on the back had followed such an attack. He (Dr. Barker) had seen another case of the kind in a young man and that had begun within a few weeks of an acute follicular tonsillitis. The histology suggested that the dermatosis was of toxic origin. He thought that it was putting the cart before the horse to suggest that the temperature in Dr. Goldsmith's case was due to the inflammatory reaction in the skin; probably both resulted from some undiscovered infection.

The PRESIDENT said that he had a case presenting a similar condition, but with a circinate arrangement, a feature he had never observed in Schamberg's diseases.

The patient was a motor-bus driver and attributed the condition to the heat from the engine. The eruption involved both the front and back of the legs, and bore some resemblance to erythema ab igne. He (Dr. Dore) wondered whether there could possibly

be any association between Schamberg's disease and erythema ab igne, and whether exposure to heat also entered into the ætiology of the former.

Dr. PARKES WEBER said that in this case he agreed that there was true pigmentation on the legs below the knees, but the colour of the lesions above the knees was almost entirely merely telangiectatic and disappeared under pressure on the skin. Had the "biopsy" microscopical examination been made on the skin of the legs below the knees instead of on the skin of the thigh, he believed that hæmosiderin would have been found in the microscopic sections.

Dr. GOLDSMITH (in reply) said he agreed with Dr. Barber that he had probably "put the cart before the horse"; one would naturally expect the inflammation in the skin as well as the rise of temperature to be caused by some focus of infection elsewhere. It was only after failing to find any such focus that he put forward the suggestion that the raised temperature might be due to a primary inflammation of the skin.

As to the President's suggestion that heat might be the cause, he would certainly go into that question, but he felt that the distribution of the disorder and the fact that it began in such tiny specks were against that explanation. So far as he knew, erythema ab igne never began from a small point and it had a reticular arrangement.

He did not agree with Dr. Parkes Weber's findings. The greater part of the discoloration did not disappear on pressure, and the pigmentation was much more widespread than Dr. Parkes Weber had stated.

Dermatitis caused by Artificial Tortoise-shell Spectacles.—HENRY MACCORMAC, C.B.E., M.D.

The patient, Miss G. J., aged 28, has worn spectacles for many years for defective vision. Six weeks ago she purchased a pair of spectacles with what was described as a new kind of artificial tortoise-shell frame. Four weeks afterwards a well-marked erythematous dermatitis developed over the nose in a narrow band, and behind the ears, corresponding exactly to the area of contact of the skin with the spectacle frame.

The patient is shown because I believe that the condition has not so far been recorded in this country.

Dr. W. J. O'DONOVAN said that he had seen, in all, three cases of dermatitis occurring in men employed in the manufacture of artificial tortoise-shell.

Two Cases of Black Hairy Tongue.—HENRY CORSI, F.R.C.S.

Both patients are middle-aged men. Duration, twenty years and five years respectively. Symptoms, occasional mawkish taste and recently some discomfort.

The appearances are those usually described, namely, a patch of filaments up to a centimetre in length, blackish, resembling hair, and occupying the centre of the tongue, but in these two cases, many of the filaments are pale in colour. It would appear that the dark colour is of the same order as that seen in ichthyosis and other hyperkeratoses.

From records of published cases and inquiries from physicians and laryngologists it would seem that the condition is rare: those who look at many tongues have either seen only one or two cases or none at all. In most of the cases recorded some kind of organism has been found, but rarely the same organism. I was surprised therefore to hear from Dr. Mervyn Gordon that in cultures from both these cases a yeast had grown, and apparently the same yeast. The species has not yet been determined.

Discussion.—Dr. GOLDSMITH said he was surprised that laryngologists had seen so few of these cases, as he had himself seen a considerable number; at one time, indeed, he had a small epidemic of them at St. John's Hospital, Lewisham. He had had cultures made in nearly all of them, and in every case Dr. R. S. Ralph had found a symbiosis of a crypto-

coccus with a nocardia growing in very fine filaments. Often the infection seemed to begin after tooth extraction, or some injury to the mouth. The cases differed considerably in their response to treatment. Some were very obstinate, especially if the condition were superimposed upon a fissured tongue. In one case, which cleared up clinically after a short treatment, cultures were repeated several times at intervals of some months, and each time the same organisms were obtained. Yet one could not say that they represented the normal flora of the mouth because in controls they were not found. Moreover, in cases of black furry tongue there was generally an absence of the usual inhabitants of the mouth, streptococci, spirochætes, etc., the nocardia and cryptococcus being obtained in pure culture. He had usually treated them by massaging with an ointment containing an antiseptic of the carbolic group such as monsol. It was more effective than a liquid preparation. Occasionally curetting was required. Subjective symptoms were generally absent, except where there was fissuring, and then seemed to be neuritic and not amenable to surface therapy. To alleviate this, X-rays were sometimes useful.

He had shown a case of black hairy tongue with chronic glossitis at a meeting of the Section, March 15, 1928, when the bacteriology was described (*Proc. Roy. Soc. Med.* 1928, xxi, 1429).

Dr. H. W. BARBER said that he had had a case of the kind some years ago, which was investigated by Dr. Broughton-Alcock, who obtained the same organisms that Dr. Goldsmith mentioned.

Dr. H. MACCORMAC said that during the late war, for a period of about a year, a medical colleague with "black tongue" had been under his constant observation. On several occasions, although no treatment was given, the condition cleared up completely, but relapsed again. This pronounced tendency to spontaneous cure had to be taken into account in estimating the supposed efficacy of any remedy. Further, such a course of events seemed opposed to the idea of an infection with, for example, a monilia.

Healed Gangrenous Purpura of the Legs.—L. FORMAN, M.D.

Patient, a married woman, aged 50.

Seen at out-patients' department in October, 1930, having had purpura affecting the lower limbs below the knees. The purpuric areas were large, involving the subcutaneous tissues. After ten days these areas became hard and black and sloughed away, leaving deep clean ulcers which healed with the scars now visible.

The temperature was raised to 99·8° at night for three days, the spleen was enlarged three fingers' breadth below the costal margin, and enlarged glands were present in the right axilla. No evidence of any septic focus.

3.11.30.—Blood-count: R.B.C.s 4,250,000; W.B.C.s 6,400. *Differential*: Polys. 27%; lymphos. 73%; platelets 370,000 per c.cm.

11.11.30.—Blood-count: W.B.C.s 6,400. *Differential*: Polys. 44%; lymphos. 51%. Spleen much smaller.

27.11.30.—W.B.C.s 17,000. *Differential*: Polys. 33%; lymphos. 66%; eosinos. 1%.

The diagnosis was purpura in an infective mononucleocytosis or chronic lymphatic leukæmia. The increase in the white cell count perhaps makes the latter more likely.

Since the patient's discharge from hospital some further purpuric spots have developed.

The platelet count in this case was above normal, but it was estimated after the conditions had been established for two weeks, and this does not preclude a low platelet count occurring at the onset of, or preceding, the purpura. The recurrence of the purpura when the patient is up and about is commonly observed, and it is of interest that v. Horvath, in the *Deutsches Archiv*, 1928, points out that marked change in numbers of thrombocytes occurs on assuming the erect posture. Gangrenous purpura in the meningococcal cases was found to be associated with thrombosis and necrosis of the arterioles, and probably the same change occurs in gangrenous purpura of septic origin.

Dr. PARKES WEBER said that if there was any question of the patient having had infectious mononucleosis in October, one could not be sure, from the present blood-count that she now had lymphatic leukæmia (or rather, aleukæmic lymphadenosis). The blood-count corresponded to the "lymphotropic" blood-picture, which sometimes lasted for weeks or months after clinical recovery from an attack of infectious mononucleosis (glandular fever) in adults. But the patient was unusually old for glandular fever. (See F. P. Weber. "Glandular Fever and its Lymphotropic Blood Picture," *Med. Press*, London, 1930. clxxxi, p. 65.)

Clinical Section.

[*December* 12, 1930, *continued.*]

"Spondylose Rhizomélique" (Pierre Marie).—F. PARKES WEBER, M.D.

This case is shown as an extremely typical example of the type of chronic ankylosing vertebral disease which Marie termed "spondylose rhizomélique"—because when the extremities likewise become affected their *roots* (that is, the shoulder- and hip-joints) are involved first. In the present patient, a thin, pale man (G.R.), aged 33, born in England of Russian-Hebrew origin, the movements in the shoulder- and hip-joints are already limited (especially in the left hip-joint) and there is apparently no movement at all in any part of the vertebral column, excepting limited movement of the head. The patient's appearance and attitude when standing, with the head and shoulders bent forwards, are characteristic (fig. 1). There are no abnormal nervous symptoms excepting that the tendon reflexes are

FIG. 1.—"Spondylose Rhizomélique."

all extremely active. The urine is free from abnormal constituents. The blood-picture shows slight anæmia of ordinary (so-called "chlorotic") type. All the patient's teeth have been removed. As Dr. Weber believes is usual in such cases, there is no history of any venereal disease and the blood-serum gives negative Wassermann and Meinicke reactions. In regard to the onset of wet weather the patient is a "living barometer." The patient enjoyed good health till after he was discharged from the Army in 1917, when he was told that he would be more useful in a civil capacity than as a soldier. After that he began to have slight rheumatic-like pains, but since 1921 the present affection has gradually developed, without any fever and practically without pain, excepting in his left hip and thigh, and even that disappears on resting and during fine dry weather. He has never had anything like rheumatic fever or acute or subacute infective arthritis. Dr. E. J. H. Roth reports on the radiograms: "There is evidence of changes in the cervical, dorsal and

lumbar vertebral joints. Definite bony bridges are seen extending over the intervertebral discs from the cervical region down to the second lumbar vertebra (fig. 2). The hip-joint presents a normal appearance. No changes are seen in the lungs."

The resemblance of this case to those previously figured by Dr. Weber is most striking (see *Proc. Roy. Soc. Med.*, Clinical Section, 1914, vii, p. 144, fig. 1; *Med.*

FIG. 2.—"Spondylose Rhizomélique."
Skiagram showing bony bridges extending over intervertebral discs.

Chir. Trans., 1903, lxxxvi, plate ii). In this disease there is probably an inborn constitutional tendency to ossification of the fibrous ligamentous structures of the affected articulations, analogous to that of the skeletal muscles in so-called myositis ossificans, in which traumata and true inflammation act merely as exciting agents.

In other words, my idea of the pathology of "spondylose rhizomélique" is that it is not essentially an infective or even an inflammatory affection, but is a progressive ankylosis due

to (*sit venia verbo*) an ossifying *fibrosis* of the ligamentous *fibrous tissue* of the joints, of constitutional origin. It may even be familial, as is shown by the cases of "ankylosing spondylitis" in brothers, recorded by A. J. Weil and Allolio (*Deut. Med. Woch.*, 1930, lvi, p. 2038), who also quote cases in twin brothers described in Ehrlich's recent monograph[1]. In regard to myositis ossificans, I would point out that even in the traumatic type a constitutional element is suggested by the fact that only very few riders ever develop a "rider's bone." The rare generalized progressive form of myositis ossificans, which is obviously dependent on an inborn constitutional factor, is a progressive ossifying fibrosis, the ossification being preceded by fibrosis, not inflammation. This was so in the case which I described with Mr. A. Compton in 1914 (*Brit. Journ. Child. Dis.*, 1914, xi, p. 497), and in the case described as one of "myositis fibrosa progressiva" by Dr. I. I. Price (*Brit. Med. Journ.*, 1930, i, p. 1131). Dr. Price has kindly informed me that the patient (a girl, aged 3½ years) has since then developed radiographic signs of ossification in the muscles.

Six Cases of Parkinsonism, with Investigation of Speech Defects and Description of a Graphic Method of making Speech Records.—E. STOLKIND, M.D.

(I) Patient, female, aged 21, single, came to the West End Hospital for Nervous Diseases in 1928, complaining of rigidity of body and limbs, and difficulty in walking. Spoke very indistinctly.

History.—In 1924 had period of drowsiness lasting three weeks; during this time, however, she attended school. Speech became slow about two and a half years afterwards. Face became expressionless. Next development was tremor of hands followed by tremor of legs, and excessive salivation.

Present appearance.—Face is mask-like. Pupillary reaction, sluggish. Rigidity of head, neck, trunk, and limbs. Coarse tremor of hands, arms, legs; loss of associated movement. Patient is losing weight. Her gait is festinent and stooping. Patient is of fair intelligence, but unable to answer questions, as she is almost completely incomprehensible. Speaking tires her quickly. She can sit for days without trying to speak. Her soft palate does not usually move.

(II) Boy, aged 13, became ill suddenly in April, 1924.

July 3, 1924.—Admitted to hospital, where he was noisy at night until his discharge. In 1927 a weakness in left arm became apparent, and a year later in left leg. Drags left leg and stoops. Tremor and rigidity in left arm and leg. Saliva dribbles slightly. Face mask-like; blood calcium is 11·1 mgm. per 100 c.c. of blood. Wassermann reaction, negative. Patient is intelligent, and goes to school. No behaviour disorder. Speech slow and expressionless.

(III) Patient, male, aged 27. Eleven years ago had "influenza." Was restless at night; was in bed for about ten days. Gradually speech became monotonous; mouth was generally open and tremor developed.

Tonsils and adenoids—to which slowness of speech and open mouth were attributed—were removed. No improvement in either after operation. Patient became increasingly worse. When he came to hospital, I found signs of the Parkinsonian syndrome. Speech slow, hesitating and unintelligible. Drags left leg; left arm is almost fixed in a rather bent position. His condition has been more or less stationary for about nine years.

(IV) Patient, male, aged 22. Eleven years ago had "rheumatic fever" (epidemic encephalitis): high temperature and pain all over body. Recovered, but fell ill six years ago. In hospital Parkinsonian syndrome was discovered; mask-like face; monotonous, indistinct speech. Three years ago weakness of the left side of the face and facial tremor; slight weakness of right eye on convergence. Coarse tremor of tongue, stiffness and tremor of the arms and legs.

He is becoming worse; tremor and stiffness have increased; he is always sleepy

[1] Dr. Weber thinks that some cases of the so-called "Bechterew" type are incomplete cases of the "Pierre Marie" type.

and sometimes cannot speak at all. Takes a long time to produce his words. Soft palate scarcely moves on phonation. Periods of "blindness" due to ocular myoclonus sometimes last four hours. Typical gait.

(V) Patient, female, aged 23. Does not remember any previous illness. In June, 1927, noticed that voice was becoming fainter. Two months later lost her voice suddenly.

Later on speech returned but voice was "hoarse and weak" (at one time she spoke very clearly and even recited). She came to the hospital complaining of her voice and nerves. She often feels a "lump" in her throat. No signs of the Parkinsonian syndrome present during the first year of illness. Speech was investigated and found to be abnormal.

As a rule she drawls in a low, colourless voice, but when she is angry she speaks hurriedly and her voice sounds more normal. Sometimes her speech requires an effort. When interviewed in hospital speaks better than when at home.

On examination (Dr. L. R. Yealland and exhibitor).—Expressionless face, tremor of both hands and of tongue. Stoops after sitting for a long time. Right arm does not swing when she is walking. There is poor convergence.

All these indicate that this is a case of Parkinsonian syndrome (post-encephalitic paralysis agitans), in which the first symptom was the abnormalities of the speech.

(VI) Patient, male, aged 20. Does not remember any previous illness. About four years ago noticed that speech was becoming difficult, monotonous, and slow. Tonsils and adenoids removed but no improvement of speech resulted. Soon afterwards patient noticed that his right hand trembled. *On examination* (Dr. L. R. Yealland and exhibitor) Parkinsonian syndrome diagnosed. Quantity of saliva in mouth. Head is slightly fixed; face mask-like. Tremor in right arm and hand, also in tongue. Slight tremor in right leg; and some rigidity in both right limbs. Power of convergence is poor.

Comment.—In cases of the Parkinsonian syndrome the affection of the speech may be so pronounced as to cause complete dumbness. I had a case of a woman, aged 23, who became very stout. Eight months after her "complete recovery" from epidemic encephalitis, the Parkinsonian syndrome developed, with slow monotonous speech. Before her death she gradually became very emaciated and dumb. Sometimes the nurse was able to understand her desires from the slow movements of her lips. The tongue, soft palate and vocal cords showed no movement.

In the case of two brothers, aged 18 and 20, the Parkinsonian syndrome developed after vaccination. There was no previous illness. The elder, who still follows his profession as a dancer, speaks slowly and monotonously; the other is much worse and is almost unintelligible.

On the other hand, one of my patients with this condition sang very frequently at home and even sometimes in the street.

Usually the speech is slow, hesitating, monotonous, unintelligible, sometimes spasmodic and quite incomprehensible, and this sign may appear in advance of any others.

A speech record is made on a special Marey-Rousselot instrument improved by Scripture.[1]

As this is the first attempt to make records of the speech of patients suffering from Parkinsonism, I show here a chart, with a chart of the normal speech for comparison.

The sentence spoken is "I'd like to go home." In the normal graph the melody is seen to rise and fall, but in the other there is (1) extreme slowness of speech, (2) monotony, and (3) a marked lack of small fluctuations.

1 E. W. Scripture, "Anwendung der graphischen Methode auf Sprache und Gesang," 1927.

FIG. 1.—Normal.

The normal inscription begins with the waves for the vowel. This is followed by the records for the other sounds.

FIG. 2.—Post-encephalitic paralysis agitans.

In this inscription the waves are extremely small owing to the high pitch of the voice. All the sounds in this inscription are greatly lengthened.

As a rule, when examined, the soft palate and vocal cords (abduction and adduction) are movable, even in advanced cases, especially after a word of command. At other times, when speaking, the movements are diminished. The speech disturbances are due to rigidity of the muscles of the larynx, fauces, tongue, etc.; in some cases there is in addition dissociation of the speech function.

[I am indebted to Mr. Lionel Colledge for the laryngoscopic examination and to Miss F. Janvrin for the making of the records.]

Still's Disease.—L. HARTSTON, M.D.

Patient, a girl, aged 13. History of several attacks of "rheumatic fever" between 1924 and 1928. Since the last attack, two years ago, she has suffered continuously from painful swelling of nearly all her joints. The condition has been progressive in spite of treatment at various institutions, and she has been bedridden for the past two years. She first came under my notice in August, 1930, having a painful fusiform swelling and limitation of movement of shoulders, elbows, wrists, interphalangeal joints of both hands, hips, knees, and ankles. Marked general wasting. Liver and spleen moderately enlarged, smooth, not tender, and easily felt. Enlarged non-tender lymphatic glands were palpable in both sides of neck, axillæ, and groins. No abnormal physical signs detected in heart, lungs, or central nervous system. Temperature while in bed without treatment was from 98° to 103°.

Pathological reports. (*Dr. H. A. Ash*).—Fluid from left elbow-joint . . . . "Purulent fluid. Film shows pus, but no organisms. Culture sterile. No tubercle bacilli found."

Blood-count: Hb., 50%; R.B.C.s, 3,800,000; C.I., 0·61; leucos., 7,800. *Differential*: Polys., 68·5%; lymphos., 25·5%; large hyals., 4%; eosinos., 2%. Poikilocytes present. Wassermann reaction in serum, negative. Urine, clear.

Radiological examination.—"Rarefaction of skeletal bones in neighbourhood of joints, with irregularity of surfaces of femoral heads and acetabula. Formation of periosteal new bone round proximal phalanges of hands. Heart shadow larger than normal, globular, and centrally placed."

Treatment.—Two intramuscular injections, each of 20 c.c., of streptococcus antitoxin were given, with an interval of three weeks between them. Each injection was followed by a severe general reaction with high fever, lassitude, increased joint discomfort, and a morbilliform rash. The whole reaction lasted up to four days, and was followed by a maintained normal temperature and a remarkable general improvement. A month after the second injection a similar injection was given, but using normal horse serum instead of antitoxin. This, too, was followed by a severe reaction, which was again succeeded by a marked general improvement. Since then the pain has rapidly diminished, the joint swellings are subsiding slowly, and there is no pyrexia. The patient is able to knit, and can walk with the aid of crutches. Improved appetite and gain in weight have been noted since treatment. The enlargement of the spleen and liver has been unaffected, but the lymph glands appear to be smaller.

This is undoubtedly a typical case of Still's disease, in which improvement has resulted from treatment by "protein shock." Still, in his original description of this condition, mentions that improvement might follow accidental complications such as measles, scarlet fever, and catarrhal jaundice. Thursfield reported a case in which apparently permanent improvement followed intravenous protein (T.A.B.) therapy. Rossdale at a meeting of this Section[1] demonstrated a case in which there was gradual complete recovery after an attack of nasal diphtheria. The improvement in this case may reasonably be ascribed to the reaction produced by diphtheria antitoxin used to treat the nasal condition.

Pulmonary Asbestosis.—PHILIP ELLMAN, M.R.C.P.

Patient, R. R., female, aged 33, worked in an asbestos factory from 1916-1921. Quite healthy previous to working there; never had chest trouble. In 1919, cough and dyspnœa developed and became worse, but patient continued her work until 1921; was then compelled to give it up. Notified as a case of pulmonary tuberculosis in 1921. Weight then was 8 st. 7 lb. (it is now 7 st. 12 lb.) She has twice been in a sanatorium. Sputum examined on numerous occasions; was never positive.

I first saw her on May 22, 1930. She was thin and emaciated. Poor chest expansion. She then had cough, dyspnœa and occasional sweats.

Chest.—Definite physical signs in both lungs. Impairment, poor movement, V. R. and V. F. + +; dry, crackling, scattered crepitations throughout both lungs, especially marked in left.

Heart was drawn over to left side. Findings typical of pulmonary tuberculosis with basal fibrosis, but in view of repeated negative results and of the nature of patient's occupation, the sputum was carefully examined for me by Dr. Schuster at the Royal Chest Hospital, June 20, 1930, when "asbestos bodies" were found; these have been found in further specimens.

Skiagram of chest shows an infiltration of both lungs which appears to be characteristic of this condition.

> *Radiologist's report* (Dr. Stanley Melville).—"Diaphragmatic movements poor. There is evidence of basal pleurisy. Heart and mediastinum displaced to the left side. Both lungs show punctate mottling distributed generally, but the situation is not that of ordinary pulmonary tuberculosis. The appearances are strongly suggestive of a trade pneumoconiosis."

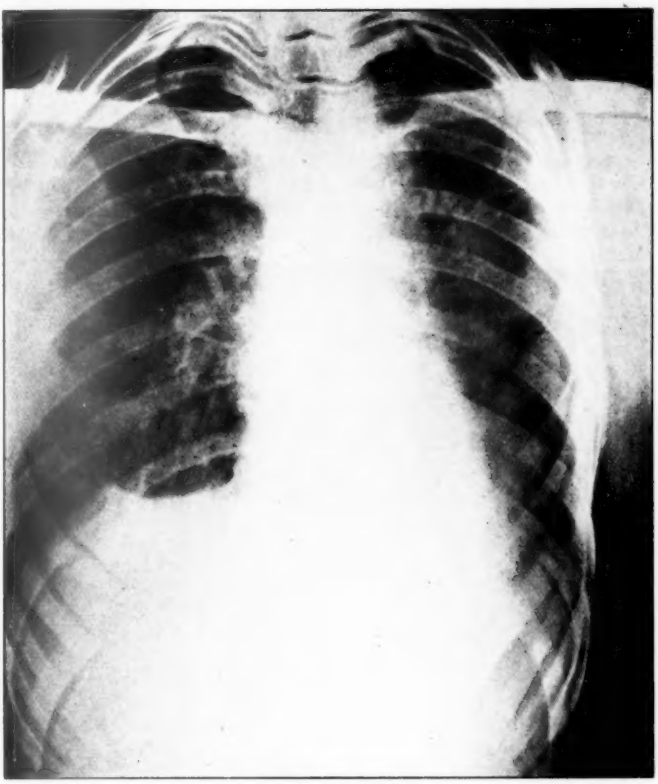
It has not been recognized until comparatively recently that a pneumoconiosis may result from the inhalation of asbestos dust, and asbestos factories have taken little precaution against it.

W. E. Cooke has estimated that there is a high percentage of silica (40%) in asbestos, and Kettle, describing "the relation of dust to infection," states that the degree of harmfulness depends upon the amount of free silica, although he

[1] *Proceedings*, 1928, xxi, 431 (Clin. Sect. 43).

considers that the silica is present in asbestos as a complex "silicate," which is apparently rather less harmful than free silica.

Symptoms and signs.—In my cases the onset of symptoms has usually been about five years after exposure to the dust, beginning with a cough, with little expectoration, and accompanied by dyspnœa, both of which become progressively worse. There is always some wasting, sometimes quite marked, and the physical signs are usually those of a basal fibrosis to begin with, followed by extension of the infiltration upwards, but affecting mainly, as in Dr. B. Wood's cases, the lower and middle zones. The heart and mediastinum are drawn over to that side where the



Pulmonary asbestosis. Skiagram showing characteristic fine diffuse fibrosis.

degree of fibrosis is most marked. The adventitious sounds are of a dry, crackling nature, and are probably due, to a great extent, to friction from the accompanying basal pleurisy.

Radiological appearances show a progressive, fine, diffuse fibrosis tending to affect the lower and middle zones. Dr. Melville has described the infiltration in this case as a "fine punctate mottling," and this fine quality of the shadows appears to be characteristic of the other cases described. A basal pleurisy is common to most cases, and, as Dr. Wood has stated, obliteration of the costo-phrenic angle is also common.

In the case now shown there is a suspicion of an annular shadow in the left infraclavicular region, suggestive of a cavity. The asbestos fibres have strong, penetrating qualities, and commonly penetrate the skin of workers, producing asbestos "corns." Gloyne has shown that asbestos fibres can be removed from the corns with a fine needle. The characteristic golden yellow asbestos bodies may be found in the skin, sputum and lung. The prognosis, when the disease is established, is, on the whole, bad. Tuberculosis is not usually a terminal condition as it is in silicosis. Many patients die from an ensuing broncho-pneumonia, and post-mortem examination has shown no evidence of tubercle. When there is persistent absence of tubercle bacilli and a history of prolonged exposure to the dust, with signs and symptoms already outlined, a diagnosis of pulmonary asbestosis can be made.

Pulmonary Mycosis (Moniliasis).—PHILIP ELLMAN, M.R.C.P.

A. B., male, aged 56, tailor. Sent by his doctor to my tuberculosis department, as a case of pulmonary tuberculosis, 13.7.29.

Has had progressive dyspnœa for ten years; cough, with an increasing amount of sputum for five years (now 6 oz. per day). No hæmoptysis. Occasional heavy night sweats. Pain in left upper chest for some years. Progressive loss of weight during last four years (2 st.). Numerous examinations of sputum were negative for tubercle bacilli.

Present condition.—Thin and emaciated; dyspnœic. Early clubbing with ribbed finger nails.

Lungs.—Respiratory movements much restricted. Physical signs in chest are those of chronic bronchitis with basal fibrosis. Report on X-ray examination of chest (Dr. Mather Cordiner): "Appearances are those of chronic bronchitis with marked fibrosis. There is scattered mottling and blurred smearing about the lung field generally.

Dr. Schuster has kindly made a complete examination of the sputum and has reported:—

> "The sputum is a more or less homogenous, greenish muco-purulent specimen. Each one examined contains numerous bodies of a fungus nature. They are in pairs or short chains of four (with a clear halo of considerable width around them in *fresh* specimens). (See slide.) On culture every specimen yields the organisms on blood-agar, but it has been impossible so far to obtain a pure culture, as it only seems to grow when mixed with other organisms. Under cultural conditions they are larger and contain numerous granules or deeply staining ends. They are Gram-negative. The shape is various, some being quite long with tapering ends and they correspond closely with the monilia forms of other authors." (Fig. 1.)

This organism has been persistent in every specimen of sputum examined, and in none have tubercle bacilli been found. The findings are therefore comparable with those of a "primary bronchomoniliasis" as described by Castellani.

It should be remembered that the mere presence of fungi in the sputum does not mean primary fungous infection as the organisms are very commonly secondary, but where, in the absence of any other definite cause, the fungi are repeatedly present, then one should suspect a primary fungous infection of the lung. Animal inoculation of the sputum often—but not invariably—produces the lesion.

The lung of a mycotic infection seen post mortem may closely resemble that of pulmonary tuberculosis, and many cases are therefore unsuspected and regarded as tuberculous. Especially is this so in moniliasis, blastomycosis, and actinomycosis and aspergillosis, and it may be only through a mycological examination of the sputum that the true diagnosis is made.

Monilia causes, in fact, a type of chronic broncho-pneumonia. The clinical condition, in contrast to tuberculosis, is characterized by the fact that the patient is not so ill and has milder symptoms. The fungi as secondary invaders probably

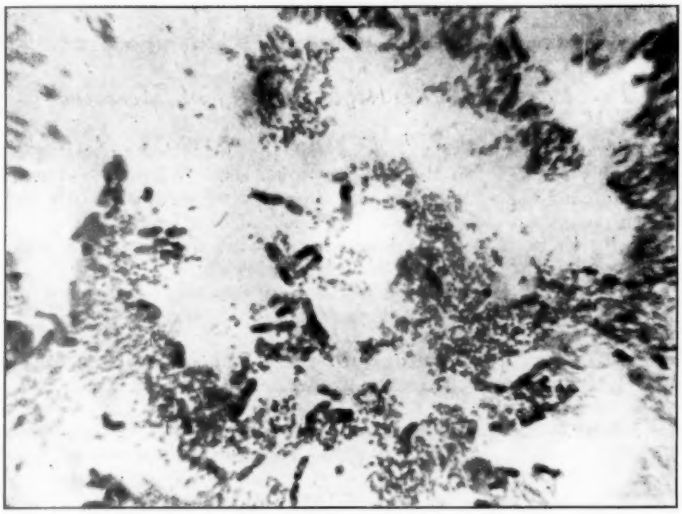


FIG. 1.—Moniliasis.
Photomicrograph of a specimen of sputum from culture, showing the long rod-shaped monilia bodies with deeply staining ends.

FIG. 2.
Note the blurred smearing about the lung field generally, and dilatation of the basal bronchi (shown also in skiagram taken after lipiodol injection) not reproduced.

contribute to the chronicity of the disease. Finally, large doses of potassium iodide are often strikingly beneficial in the primary mycoses. In the secondary infections occurring in pulmonary tuberculosis, the pulmonary tuberculosis often improves by treatment with potassium iodide.

Radiologically there is a blurred smearing about the lung-field generally, in contrast to the well-defined appearances of a coniosis (fig. 2).

I am indebted to Dr. Saxby Willis, who kindly saw this case with me, for many helpful suggestions.

Pulmonary Tuberculosis with Painless Ulcer of Tongue and Marked Wasting of Left Pectoral Muscle.—PHILIP ELLMAN, M.R.C.P.

S.D., male, aged 30, carpenter.

Previous history.—Fractured base of skull, with left-sided hemiplegia, 1909; pleurisy with effusion, 1915; notified pulmonary tuberculosis, right apex, 1917; treated for tubercular abscess of hand at London Hospital, March, 1928; ulcer developed on dorsum of tongue, December, 1927.

Present condition.—Active bilateral infiltration of both lungs with cavitation. Marked retraction of left side of chest; pectoral muscle on that side remarkably wasted (? cause).

Large ulcer on dorsum of tongue; this is painless providing no highly seasoned food comes in contact with it. A similar case was shown by Mr. Cecil P. G. Wakeley at a meeting of the Section in February, 1930.[1]

The cause of the wasting of the left pectoral is of considerable interest in this case. I myself have considered it to be congenital absence of the pectoral with the mere presence of a fibrous tag. Other suggestions—such as (1) The result of an unrecognized poliomyelitis, (2) a muscular dystrophy, (3) the result of the old hemiplegia—cannot be definitely dismissed.

Discussion.—The PRESIDENT said that during the last three years a series of painless ulcers of the tongue had been shown at meetings of the Section.

Mr. ERIC CROOK said he thought that the question of painlessness or otherwise was due to the position of the ulcer in the tongue. Ulcers which were on the tip of the tongue were rather more sensitive than those on the dorsum.

[1] *Proceedings*, 1930, xxiii, 601 (Clin. Sect. 51).

Section of Epidemiology and State Medicine.

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Recent Views on Pneumonoconioses.

By Edgar L. Collis, D.M.

Abstract.—Silicosis has been intensively studied since it was isolated from other diseases caused by dust. These studies have shown that silicosis may be fairly advanced without seriously impairing general health; it may, however, itself lead to a fatal result. More often it acts almost specifically in preparing the way for pulmonary infections, of which serious tuberculosis is the chief. The occurrence of such a superadded infection not infrequently precipitates a latent condition of silicosis. The close relation existing clinically between tuberculosis and silicosis has been demonstrated by animal experiment.

Other dusts than silica have also been demonstrated to cause generalized pulmonary fibrosis, which is usually finer in character, although more injurious to the functions of the lungs than is silicosis; but such fibrosis has not been found to be specifically associated with superadded tuberculous infection.

Each dust calls for special study. Up to the present, investigation of dusts from certain silicates has shown them to be of great importance. Of these, asbestos has been found to be most definitely injurious, and to originate a definite and characteristic condition. Other silicates, such as basalt, appear to set up a condition which only differs in degree from that caused by asbestos.

Dust arising from pure coal does not appear to be injurious, or, on the other hand, to be in any way protective against infections. Raw coal, however, often contains sufficient minerals for its dust to originate pulmonary fibrosis. When such fibrosis is present, whether due to silica arising from intervening rocks or from silicates, the coal particles are so retained in the lungs as to block the lymph passages, and impair capacity.

Certain other dusts, for example dusts arising from marble or limestone, exert little, if any, influence on the lungs. Such dusts are soluble in the body fluids, and are not left to block the pulmonary tissues.

Much work in recent years has been done upon the group of diseases known as pneumonoconioses. The studies have generally been industrial and epidemiological, or experimental, in which industrial dusts have been used. These lines in investigation may be said to have started [6] when silicosis, as a separate industrial disease, was picked out from the group by the use of statistics. This step was made possible by noting that wherever in industry a high mortality from dust phthisis was present, a silica risk was also present, and by noting that no such high mortality from dust phthisis could be found in dusty industries when silica was not present in the dust. While research has, during the past twenty years, tended to centre upon silicosis [10], definite evidence has been gathered and is accumulating, that other dusts than silica, for example, that of asbestos [27], bring about definite pathological changes in the lungs, even though the disposition to succumb to tuberculous infection, so characteristic of silicosis, may not thereby be produced.

This paper is an effort to summarize recent work which has been done according to the industrial hazard under investigation. No effort is made to repeat long-accepted data which have remained unchallenged. It is merely a progress report.

Silica Dust.

Incidence.—It has been generally agreed, not only in this country but abroad, that the old-time diseases known as miners' phthisis, potters' rot, grinders' rot, masons' rot and knappers' rot, arise in every case from exposure to the inhalation of silica dust generated in industry [6]. Further, investigations have shown that the disease, now known as silicosis, is found wherever there is a silica dust hazard, as,

for instance, in the granite industry [18]. In this last-named industry, where the dust is only composed of about one-third silica, so long as the hammer and chisel were used, the disease was not generally recognized; but when, with the introduction of pneumatic tools for cutting and carving, much more dust was generated, the disease became manifest both in this country and in the United States. Investigations have been carried out in both countries, and particularly in America, where the mortality from respiratory diseases among granite cutters has been shown to have been increasing steadily during the present century until it is now fittingly described as appalling. In fact, here and in other occupations, silica dust may now be said to be recognized as an industrial hazard of the first importance, just as much as the dust of lead or other toxic substances.

The most reliable of recent data throwing light upon the whole subject of dust diseases are those contained in the Registrar-General's Decennial Supplement dealing with Occupational Mortality, which was published in 1927 [30]. While reinforcing all that was already known with regard to the harmful character of silica dust, the data it contains suggest that this dust is even more generally harmful than had been supposed. They also point to other dusts, but by no means to all dusts, as originating respiratory mortalities, which, however, differ distinctly from those caused by silica. For convenience the information therein contained may here be briefly summarized for all dusts. The association between various respiratory diseases and exposure to dust is an old one, and it is re-established by finding a strong positive correlation between mortality from respiratory tuberculosis and bronchitis, and also from pneumonia. This correlation would appear to depend upon the mortalities prevailing in industries with a silica dust hazard, in which all these three respiratory diseases are found in excess. Nevertheless, bronchitis may be high, as among cotton strippers and grinders, with phthisis low; while phthisis may be high, as among slate masons, with bronchitis low [33 and 36]. These instances, however, are exceptional where dust is the causative factor.

The outstanding features of mortality [11] in a group exposed to any harmful dust are an excessive mortality from bronchitis and a raised mortality from pneumonia, which mortalities, when the dust is composed wholly or in part of silica, are characteristically associated with an unusually high mortality, occurring late in life from "phthisis"—a term used to include pulmonary tuberculosis and chronic interstitial pneumonia. This association with tuberculosis distinguishes silicosis from other forms of pneumonoconiosis.

This specific mortality, found associated with a silica-dust hazard, suggests that silica dust sets up a chemical reaction in the lungs, rather than a mechanical irritation. Here it may be recalled that silicon and carbon are fraternal elements, that silica is slowly converted into a colloidal hydrate in an alkaline solution such as the body tissues provide, and that under such conditions the silica might be expected to displace carbon from the protoplasmic molecule; certainly, in the field of geology, when in contact with organic structures, either animal or vegetable, silica does so enter into and replace carbon compounds as to form silica fossils, with every minute anatomical feature faithfully reproduced, whether it be of trilobite or coal tree.

Great care has been taken in the presentation of the recent records for English occupational mortality in order to give them a stronger occupational, in contrast to an industrial, bias than heretofore. This point gives weight to a somewhat unexpected association disclosed between dust hazards and diseases of the cardio-vascular system. Thus, out of the 178 occupational groups dealt with, among the ten highest in order of mortality from cerebral hæmorrhage are to be found five with dust hazards, arising from metalliferous mining, raw cotton, and sandstones; among the ten highest in order of mortality from valvular disease of the heart are to be found seven with dust hazards, arising from raw cotton, slate, and sandstone; while

among the ten highest in order of mortality from "other" heart disease, chiefly myocardial, eight have definite dust hazards, arising from metalliferous mining, sandstones, ground flint, and raw cotton. Further, some association seems to exist between dust hazards and chronic nephritis, which may account for the existence of a significant correlation between mortality from bronchitis and chronic nephritis. The suggestion emerges, since occupations with a silica hazard stand out first in these instances, that silica dust may induce degenerations in other tissues than those of the lungs. But, if this idea is accepted, the same suggestion must be entertained for the dust which arises, or used to arise, in cotton carding rooms, and originated cotton-strippers' asthma. A simple explanation would be forthcoming if the pathological conditions in the asthma cases were those of silicosis, and were associated with such high mortalities from tuberculosis as are characteristic of silicosis. These conditions, however, are not present: nor is silica clearly present in the dust of the carding rooms.

The conclusion to be drawn must be that other dusts than silica can both harm the lungs, though not necessarily in the same way, and also lead to degenerative changes in the cardio-vascular system. Such a conclusion has not yet received full pathological support, possibly owing to concentration upon the characteristic pulmonary lesions in these cases, while only subsidiary attention has been paid to the presence or absence of degenerative changes in other organs.

No less important than the additional evidence forthcoming from these occupational records to incriminate certain dusts already on the black list is the lack of any such evidence for condemning limestone, cement or brick-clay—to fine dusts of which exposure readily occurs in certain occupations—or for bringing to light some harmful dust not previously suspected.

The English occupational mortality records give no useful information regarding exposure to granite dust, because the amount of this rock occurring in England is inconsiderable; but information from Aberdeen, where local and imported granites are largely dressed and carved, has shown [6] that the dust, rather less than one-third of which consists of silica in the form of quartz, sets up silicosis. A few additional observations have quite recently been put on record which establish clinically the existence of silicosis among granite workers [32].

We have, however, to turn to the United States of America for full information as to the extent of the dust hazard caused in the granite industry, and to the incidence of the resulting mortality [18]. Perhaps the most interesting conclusion drawn is that about twenty million fine particles of granite dust per cubic oot in the atmosphere represents a threshold below which harm does not result. Somewhat less than one-third of this dust is composed of free silica, hence this harmful threshold agrees fairly closely with one of six million particles suggested from the South African gold mines, where free silica is the only constituent of the dust.

Although no evidence was gathered for this last-mentioned report on the granite industry, as to the incidence of tuberculosis among those in contact with tuberculous silicotics, this subject was approached in an earlier report on the industry [20], wherein the disease was found to be comparatively rare among contacts. Thus support was given to the view, often expressed, that tuberculous silicosis is less infectious than ordinary pulmonary tuberculosis. This view, however, has been controverted by Heffernan, who failed to find evidence in its support [19]. Nevertheless, the suggestion has been made by the South African workers, approaching the matter from a different angle, that silica may actually damage the bacillus, so as to lower its virulence. Exposure to dust in the granite industry has increased greatly since pneumatic tools were introduced about thirty years ago; with this increase the mortality from pulmonary tuberculosis among American granite cutters rose from 1·5 in 1890-95 to 14·7 in 1920-25, and to 19·5 in 1924-26. Possibly even higher

mortalities are yet to be recorded, since there is always a period of lag before the effect of any reduction in the dust risk becomes manifest—a period during which those already silicotic are developing tuberculosis.

The existence of this period of lag has been well established by the careful records published annually by the Miners' Phthisis Medical Bureau of South Africa [29], whence it appears that from six to seven years must elapse during which cases may be occurring with increasing frequency among those who were exposed to harmful conditions of work existing previously, even though these conditions have since been materially improved.

Since the suggestive evidence gathered from the manufacture of second-grade ganister bricks [7], no further facts have come to light in support of the idea that inhalation of silica dust can ever be innocuous. Miners in quartz rocks at Cripple Creek in America, who were at one time claimed to be free from the disease, have been found to suffer from silicosis; although, as dyspnœa develops, the men are unable to stay at that mountain height, and so many have to leave the mines before silicosis has fully developed. Another instance quoted has been the Mysore gold mines in India; but here investigation has disclosed that although silicosis is not known to have been caused, there is no silica dust risk present to cause it, since the mother rock in which the narrow metalliferous lode runs is not composed of silica.

Another dust shown [33, 36] to set up a silica hazard is that of slate, which contains from 50 to 80% of fine quartz and about 10% of silicates. Unduly high mortalities from phthisis occurring late in life, associated with high mortalities from bronchitis and pneumonia, were found among slate workers, together with clinical indications of the existence of pulmonary fibrosis and silicosis.

A further noteworthy occurrence with regard to the incidence of silicosis has been that of certain fatal cases recorded as acute silicosis [23], following upon comparatively brief exposures of about four years to dust composed of 75% silica with 25% of sodium carbonate and soap. Here the course of advanced tuberculosis which was present seems to have been enhanced by the inhaled silica; while the solubility of the silica particles may have been accelerated by the alkaline dust inhaled at the same time, with the formation of nodular fibrosis. The lungs in these cases were bulky and heavy, preserving their anatomical shape; they were tough, and grated when cut. They recalled the bulky, massive lungs seen among metalliferous miners thirty years ago, when the dust hazard in the mines was excessive.

Clinical findings.—Evidence, chiefly from South Africa [37], has established that when once a lung has been dusted with silica it tends to develop silicosis, even after all exposure to the dust hazard has ceased for some years. Further, the prognosis for a group of cases of simple silicosis at the end of ten years is about the same as for a group of cases of pulmonary tuberculosis; this unfavourable outlook is chiefly due to the supervention of tuberculosis upon a silicotic condition.

But, apart from infection with tuberculosis, other pulmonary infections, such as those which result in pneumonia, broncho-pneumonia or bronchitis, may supervene; or the case may terminate comparatively suddenly from cardiac failure, due possibly to myocardial degeneration.

Many cases have now been watched in South Africa while simple silicosis has been progressing. They have, until an advanced stage is reached, exhibited little, if any, interference with general health and nutrition, and, except for dyspnœa on exertion, have experienced no incapacity for work. Clearly, any degenerative changes induced by silica do not paralyse functional activity. Clinically, the existence of such changes is manifested by the tendency to succumb to infections, of which tuberculosis is the most characteristic.

Recently French observers [31] have stressed the fact that considerable exposure to silica dust in mines may be experienced for ten years or more without setting up

pulmonary silicosis; a quarter of such miners, on examination, may present no abnormal clinical or X-ray signs.

On the other hand, South African evidence indicates [26] not only that silicosis prepares the lungs to succumb to tuberculosis, but that tuberculous infection will precipitate a "latent" silicosis. The suggestion has even been made that an infection has always been present where silicosis develops, as though the pulmonary tissue required such infection to enable it to react with the silica.

X-rays.—A hope was entertained at first that X-rays would provide accurate means for detecting silicotic fibrosis during life. Much work has been done on the subject, which has led to recognition of the fact that changes set up in the lungs by other dusts than silica may, on X-ray examination, be indistinguishable from those produced by silica dust. This finding, of ccurse, does not mean that the condition which throws similar shadows is, in fact, similar. Fibrosis, rather more diffuse than is usual in cases of silicosis, may be present, but this form of fibrosis has not been found to predispose the man to tuberculous infection in the same way as occurs in the case of silicotic fibrosis [6A and 5]. Nevertheless, the progress of silicotic fibrosis can be watched by X-ray examinations, which, when a group of workers exposed to a silica dust hazard are being medically supervised, is of first-rate value [38]. Attention for the moment is being directed to establishing a recognized technique for radiology of the chest, for which a standardized position of the patient, the moment in breathing, distance of the tube and the type of rays, should be fixed. One point has emerged, viz., that men with cylindrical or vertical heart shadows are particularly liable to fall victims to tuberculosis if exposed to a silica dust hazard; while in those who have subsequently succumbed to the infection the heart shadow tends to change to the cylindrical type.

Pathology.—Much careful work has been done, and the course of silicosis as it develops has been followed and described with minute and praiseworthy detail [38]. But little practical knowledge has arisen therefrom, since Macrae established the size of dust particles which must be considered harmful, since they are found plentifully distributed throughout the lung tissue. They are of the same group size as tubercle bacilli, only a few exceeding five microns in diameter; the majority are about one micron. The suggestion has been advanced, particularly by Watkins-Pitchford [37], that the presence of the tubercle bacillus is necessary from the start to initiate the fibrotic reaction between the silica and the tissues, and so that every fibrotic nodule has a bacillary nucleus. Such a nodule, by breaking down, may later release the infection. Or a new infection, usually by inhalation, may occur. In either case the silicotic nodule forms an attractive nest for the bacilli.

Laboratory research.—Activities under this heading have recently been so ably summarized [22] by Professor E. H. Kettle, in his presidential address to the Section of Pathology, that extended reference here would be out of place. Two lines of work, however, stand out. In the first, L. U. Gardner, who experimented [15] with guinea-pigs and used a strain of tuberculosis with low virulence and granite dust, concluded that tubercles occur more frequently in dusted than in undusted lungs, and that the lesions produced, instead of healing, run a more prolonged course. When marble dust was used, it mostly dissolved in the lung tissues and helped to calcify any tuberculous lesions present; while any silica particles in the marble set up silicosis which caused the low virulence strain of tuberculosis to pursue an unusually chronic course delaying the process of resolution. Later, Gardner, using the same strain of tuberculosis, has shown [16] that dusts of granite and carborundum, but more particularly of quartz, will stimulate the renewed multiplication of bacilli in healing tubercles. Hence the suggestion is made that industrially inhaled dusts of the proper type may light up pre-existing quiescent foci of infection or disease, as well as so modifying the lung tissue that they more readily fall a prey to infection. Dusts of marble or coal had no such stimulating or reactivating effect.

Then comes Kettle's own work, which has been of great interest. It is directly continuous to a previous demonstration that a culture of pure tetanus will not affect the human body unless it is injected together with either calcium salts or silica; and is complementary to the work of Gardner. Kettle has shown that when necrotic foci are induced in mice, tubercle bacilli settle and multiply much more rapidly in the foci caused by silica than in those due to the injection of any other substance. These two lines of research are remarkable in that through them a relation has been shown to exist between the growth of tubercle bacilli in living tissues and the presence in those tissues of silica. This laboratory research gives support to clinical findings and mortality records from industries which display this connection as something peculiar to the inhalation of silica dust. The way in which dust particles of all sorts are picked up in the alveoli by macrophages or dust cells, and by them are finally, perhaps months or even years later, carried into the lymph channels of the lungs, has been studied especially by Carleton [4] and also by Mavrogordato [24 and 25]. Different dusts are engulfed with different zest by the cells, and silica particles appear to be quite unattractive. Since the mobility of dust cells is impeded by a heavy burden of particles, this factor may leave cells which hold only a few silica particles with greater mobility. On the other hand, Mavrogordato holds that silica particles slowly disintegrate in the cells, poisoning them but preserving them like mummies. Such dead phantoms drift to the nearest lymph node where they collect, blocking up the road, until they finally go to pieces among the débris which has gathered at the spot. These researches indicate that particles of silica dust in the tissues react rather differently from other particles, and that they disintegrate or dissolve rather than linger as inert foreign bodies.

Marble Dust.

Careful investigations have been made in the marble industry at Carrara in Italy [3 and 35]. Just, however, as for Portland and Bath stones in this country, fine dusts arising from these limestones, even though inhaled in large amounts for many years, have been found innocuous, possibly due to their ready solubility in the lungs. Certainly X-rays have failed to demonstrate any lesion following the inhalation of these dusts. Nor have clinical examinations nor pathological examinations brought any damage to light.

Portland Cement.

Exposure to dust has been closely studied in the cement industry [34] wherein those employed are intensely exposed to fine clouds of dust; the dust is composed largely of calcium salts and silicates. X-rays disclosed the presence of some generalized fibrosis and more calcified nodes than normal, possibly indicating protection against tuberculosis. A tendency was found to diseases of the nasal fossæ, acute bronchitis, diseases of the pharynx and tonsils, and influenza; but not to the more serious respiratory diseases. Possibly the silicates present, rather than the calcium, were responsible for such indications of trouble as were found.

Coal Dust.

The occupation of coal mining has long presented an interesting picture. The coal-miner's lungs become as black as the coal he gets, but his mortality statistics are in striking contrast to those for metalliferous miners [8 and 9]. The mortality of coal-miners in all countries from pulmonary tuberculosis has long been recognized to be low, usually as low as that for agricultural labourers. Recently a group of investigations has been carried out, some of men working in docks as coal trimmers, and so exposed to dust, others of coal-miners getting different classes of coal, others,

of men working in coal mines upon rock work rather than in getting coal, and others again, through experimenting by exposing animals to the inhalation of coal dust.

Coal trimmers.—These men [6A], working in ships' holds, are exposed to dust of coal only, without a mixture with any other sort of dust, such as from rocks between the coal measures when coal is being mined. Nevertheless, coal cannot be regarded as purely organic, since the trees of the Coal Age must have fallen into lagoon mud, which may often have contained sand. Coal trimmers suffer an excessive mortality from pneumonia and from bronchitis, but only die at about the same rate as the standard from pulmonary tuberculosis. Radiography has disclosed that, after years of work, the lungs of these men are not normal. They exhibit bilaterally extensive fine reticular shading, often associated with dense mottling; in fact, the shadows seen were similar to those which had previously been widely regarded as characteristic of silicotic fibrosis. The evidence here is clear, that lungs may be so damaged by coal dust as to become fibrotic, and hence be more than ordinarily prone to succumb to certain superimposed infections, without being more liable to tuberculous infection.

Coal mining.—The most reliable data as to the mortality of coal miners are given in successive decennial occupational supplements of the Registrar-General for England and Wales. They have always exhibited miners on different coalfields as experiencing quite diverse mortalities from respiratory diseases; thus, even though the phthisis rate is low on all fields, the Lancashire rate is double the Nottingham rate; the pneumonia rate on the whole is about normal, but here again the Lancashire rate is in excess, and is more than double the Nottingham rate; again, the bronchitis rate is well above normal, but here also the Lancashire rate is excessive, and is over three times the Nottingham rate. Other coalfields stand between these two extremes; but the outstanding feature is that the three respiratory causes of death are found varying together, being either all comparatively high, or all medium, or all low on the same field. Years ago Oliver maintained that "when a coal miner's lung shows pronounced fibrosis, it is generally an indication that the individual has worked in a coal seam which contained a quantity of stone; it is the stone dust in the coal, not the coal itself, which . . . . is the cause of the fibrosis." And in 1915 the opinion was expressed that "probably the prevalence of respiratory diseases among miners depends on the amount and character of the stone dust present." Statistical inquiry in 1922 [8] indicated that the prevalence of phthisis not only "varied on the different coalfields, but varied with the prevalence of the other respiratory diseases, pneumonia and bronchitis," so suggesting that "tuberculous silicosis may account for the diversities found." Further, statistical indications were placed in 1923 [9] before this Section that "the type of phthisis appears to be the same (as among metalliferous miners) and only to vary in intensity." These statistical deductions have now been borne out by clinical and pathological findings.

Hard heading work in coal mines.—When sinking shafts for coal, but more particularly when driving roads through sandstone rocks in order to get at the coal, a small group of miners who specialize on such work are exposed intensively to silica dust, just as are metalliferous miners. And, as might be expected, they are found to contract silicosis, and thereafter to die from tuberculous infection [39]. Interest in these cases lies in the inability of coal dust inhaled with the silica particles to inhibit in any way the toxicity of the silica. Coal dust is present in overwhelming amounts in such lungs, for it cannot get away as usual, since it becomes caught in lymph channels blocked by fibrosis. Parts of such lungs become converted into what are almost solid balls of coal [13 and 14]. Here is evidence that coal dust neither inhibits the fibrotic action of silica, nor interferes with tuberculous infection being imposed thereon. It accumulates in a fibrotic lung, acts

as a foreign body, and accentuates pre-existing silicosis; thus it may of itself lead to serious or even fatal disease. These clinical [21] and pathological findings are on all fours with experimental results obtained by dusting guinea-pigs with silica, followed by dusting with coal [24]. They indicated that once silica is fixed in the lung tissue, coal exerts no elimination effect; if anything the influence is in the opposite direction.

Coal miner's lung.—The influence of coal dust has also been intensively studied [5] on industrially healthy coal-getters, whose lungs exhibited alterations in radiological appearances developing according to duration of employment with fine or coarse mottling throughout, comparable to, but finer than, X-ray films from cases of silicosis. Such changes, even though pronounced, may be quite consistent with working health; but they represent impaired respiratory efficiency and diminished vital capacity. Men getting anthracite showed these changes more than those working semi-bituminous coal, and they also experienced in late life mortalities excessive from bronchitis, unduly high from pneumonia, but only moderately raised from pulmonary tuberculosis. The lung opacities which gave rise to the X-ray mottling were found due to fibrosis associated with an abnormal amount of silica in the lung ash and the retention of excessive coal dust in the lung tissue. The source of the silica may be sought in minerals occurring in raw coal, or in rock—or stone—dust associated with mining processes. Not less interesting than these positive findings is the comparative absence of such findings and such respiratory mortalities among hewers getting semi-bituminous coal, which appears to indicate that the dust of coal unadulterated with any mineral constituents is not obviously harmful; and that anthracosis only exists as a pathological entity when pulmonary fibrosis leads to an accumulation of coal dust.

Dust from Iron Ore Mining.

Iron is found in two kinds of mineral: one is the carbonate of iron or ironstone, and the other hæmatite or iron ore, which is oxide of iron [12]. As found, the ore contains up to 7 per cent. of free silica.

Mortality.—Dust is plentifully generated in the mines. An investigation has shown that hæmatite miners suffer unduly in late life from bronchitis, which ironstone miners do not, and the evidence of mortality statistics on the whole suggests the existence of a dust risk for these miners.

Clinical examination.—When examined medically, no definite lung trouble was discovered, although some mild nasal and laryngeal irritation was present.

Radiography.—These miners presented an interesting X-ray picture, contrasting with that seen for silicosis. The arborization from the root shadows was, if anything, rather more pronounced than in silicosis. A generalized fine mottling, like that of a spider's web, was seen only slightly developed at the apices; while the outline of the heart shadow tended to be blurred, and was reminiscent of what is seen in cases of asbestosis.

Pathology.—Definite changes of fibrotic type have been found after death among miners exposed to the inhalation of dust in hæmatite mines. These generalized fibrotic changes resemble those set up experimentally in animals when such toxic dust as lead carbonate is inhaled.

The conclusion of the matter is that prolonged inhalation of dust from iron ore does not originate miners' phthisis or, indeed, any tendency to pneumonia, but it does set up bronchitis, and causes shortness of breath, impairing chest expansion. The dust originates definite generalized pulmonary changes of a fibrotic type, which impair the usefulness of the lungs

Dust of Silicates.

The suggestion has been made [1] that dust from silicates, such as orthoclase basalt, and from other minerals, including metallic ores, asbestos, and cement, may set up a generalized fine fibrosis which is distinguishable in X-ray films from the coarse fibrosis of silicosis. This form of fibrosis is claimed to cause greater mechanical damage to the lungs than does silicosis, to prepare the way for pulmonary troubles other than tuberculosis, or even to terminate fatally of itself. While many observers regard fine fibrosis as an early stage of coarse fibrosis [38], the possibility of it being a separate pathological entity must be regarded. The existence of such an entity would explain many facts in morbidity and mortality which are otherwise difficult to grasp, such as that some dusts result mainly in high mortalities from pulmonary tuberculosis, while others give rise mainly to bronchitis and pneumonia. The two pathological entities of fine and coarse fibrosis must, however, often occur together, when a mixed type of mortality associated with high mortalities from all three diseases may result.

Asbestos Dust.

Almost suddenly a whole literature has sprung up related to the dust of the fibrous minerals known as asbestos, which are hydrated silicates, usually of magnesium, but sometimes of other metallic bases. These minerals can be split into long and flexible fibres, used for spinning and weaving, which resist heat and acids, and possess insulating properties with respect to electricity. The occupational dust-risk has been studied where asbestos is manipulated in textile factories and clinically among its victims [27 and 28]. A distinct type of fibrosis results, varying in intensity with exposure to dust, but developing fully in from seven to nine years, and capable of causing death after about thirteen years' exposure. Seen by X-rays it is finer than silicosis, and does not mask to the same extent the arborization radiating from the hilum ; the appearances are more delicate, softer and more diffuse. The nodular type, characteristic of silicosis, is not present. Pleurisy is present, but the apices of the lungs are not so adherent as in silicosis. The cylindrical heart is not often seen, and there is no special tendency to succumb to tuberculosis.

A useful diagnostic sign is the presence in the sputum and in the lungs of elongated asbestos bodies [17], which are from 20 to 100 microns in length, of a golden brown colour, varying in shape. They appear to be spicules of asbestos upon which blood-pigment and proteins have deposited. When recovered from fæces the pigment is partially destroyed by digestive juices.

Asbestos exhibits in an extreme degree the type of pulmonary impairment which the dust of certain silicates can originate. Its study has led to the recognition of a definite type of fibrosis quite distinct in origin and development from silicosis.

Nevertheless, all silicate dusts do not possess this property ; thus clays generally do not so act, although exposure to their dusts is considerable in the manufacture of bricks and of fireclay goods.

General Summary.

(1) The isolation of silica from other dusts has been fully justified by later research, which has provided evidence that (i) silicosis may be fairly advanced without seriously impairing general health ; (ii) silicosis acts almost specifically in preparing the way for serious pulmonary tuberculosis ; (iii) tuberculosis may precipitate latent silicosis ; and (iv) a close relation has been found to exist experimentally between the two conditions.

(2) Other dusts can originate generalized pulmonary fibrosis, which may be finer in character and more injurious to the functions of the lungs than is silicosis, but lacks any special association with tuberculosis.

(3) Each dust calls for special study, but those of certain silicates appear to be of great importance. Asbestos is the most characteristically injurious, but others, such as basalt, set up a condition which differs in degree rather than in type.

(4) The dust of pure coal seems to be innocuous; but many samples of coal contain sufficient minerals to set up pulmonary fibrosis. And this fibrosis causes the coal particles to be so detained in the lungs as to impair their capacity mechanically.

(5) On the other hand, pure calcium dusts, such as marble and limestone, as met with in industry, have no injurious effect. Moreover, they dissolve in the body fluids and so do not accumulate as may coal.

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Discussion.—Dr. PHILIP ELLMAN said that industrial pulmonary disease was not only of interest to epidemiologists and pathologists but it also occupied a prominent place in general practice, especially among practitioners whose patients worked in dusty trades.

He had had an opportunity during the last two years of seeing a number of cases of asbestos pneumonoconioses which had been sent to his Tuberculosis Department as suspected cases of pulmonary tuberculosis. As Professor Collis had pointed out, unlike silica dust which depended for its degree of harmfulness on the amount of free silica, asbestos dust contained no free silica but a complex silicate. Whilst silicosis produced a coarse nodular fibrosis, the fibrosis of asbestos was of a fine but diffuse nature. Nevertheless in an established case this diffuse fibrosis produced even greater mechanical effect than in a similar case of silicosis.

Speaking generally, the clinical characteristics were somewhat as follows: There was usually a history of exposure to the dust for periods varying from 5 to 15 years, and the degree of fibrosis varied directly with the length of exposure and to some extent with the process involved, viz., carding, spinning, making of asbestos mattresses, etc. It was curious that symptoms were not observed until at least 4 or 5 years after exposure. The patient was first conscious of some dyspnœa on exertion and perhaps of a dry hacking cough. These soon became persistent and progressive in nature, and after a time, following repeated colds—to which his (the speaker's) patients were peculiarly liable—the cough was accompanied in some cases by the production of some mucopurulent sputum. In only one case was the sputum stained, and hæmoptysis had never occurred. Night sweats were not uncommon, and in an advanced case there was cyanosis, particularly about the lips, and finger clubbing. The sputum was persistently negative for tubercle bacilli, but the characteristic golden yellow "asbestos bodies" had been found in a number of cases. Unlike silicosis it was apparently rare for a case of pulmonary asbestosis to develop pulmonary tuberculosis, although the speaker had a case at the present time with tubercle bacilli and asbestos bodies in the sputum, and clinical and radiological evidence of tuberculous infiltration of the lung parenchyma with increase of the basal linear striation suggestive of early asbestosis.

As Professor Stewart of Leeds had pointed out, the mere finding of asbestos bodies in the sputum did not necessarily indicate pulmonary asbestosis. If with this finding there was clinical and radiological evidence of pulmonary fibrosis, then the diagnosis was beyond doubt. The physical signs were characteristic in an established case. There was limited chest expansion, often marked wasting, impairment of percussion, especially at the bases of the lungs. The breath sounds were usually diminished, especially at the bases, there might be pleural friction at the base, and adventitious sounds of a fine dry crackling nature were characteristic. There was nearly always some evidence of a basal fibrosis and pleurisy.

The X-ray findings were also very characteristic. In his (Dr. Ellman's) cases, which had all been examined radiologically by Dr. Stanley Melville of the Brompton Hospital, the infiltration had been of a fine more or less diffuse nature in the fully developed case. The lower zone had always been affected first. Diaphragmatic movements had been limited, the picture often being characteristic of a basal fibrosis and pleurisy. The infiltration then tended to spread to the middle and upper zones. There might, according to the degree of fibrosis, be cardiac and mediastinal displacement. In the very early cases there was merely an increase of the basal linear striation.

[Dr. Ellman then showed a number of skiagrams of the chest illustrating these various points.]

Pulmonary asbestosis had now become an important industrial disease and presented points of considerable interest to the clinician. Merewether[1] had estimated that there were over 2,000 people engaged in the industry in this country. The length of exposure to the dust was of outstanding importance. The presence or absence of a system of local exhaust ventilation was also important.

Sir WILLIAM HAMER said he had been much interested in the reference made to the possibility of chemical interplay, perhaps of an actual rivalry, between the atoms of silicon and carbon. We had been told, in "The Mysterious Universe," that nothing in the physical constitution of the carbon atom was known "to account for its very special capacity

[1] Loc. cit. [27].

for linking other atoms together"; and, again, that "only a slight difference" between it and the atoms of boron and nitrogen, accounted for "all the difference between life and absence of life." And, now, silicon was apparently taking a hand in disease if not in life processes. The suggestion made by Professor Kettle, too, that tradition may have played a part in bringing about differences between death-rates from particular diseases in Lancashire as compared with other coalfields, was specially interesting, for it had for many years been apparent that North-West England and London had been influenced by differing traditions in respect of recording death-rates from two nearly allied forms of epidemic disease, to wit. scarlet fever and diphtheria.

Section of Therapeutics and Pharmacology.

[*January* 13, 1931.]

DISCUSSION ON THE THERAPEUTIC USES OF IRON.

Dr. L. J. Witts: The metabolism of iron has been the subject of many researches. The whole body contains only 3 to 3·5 grm. of iron, of which about 2·5 grm. is contained in the hæmoglobin. Traces of iron are present in all living cells, and appear to be essential for biological oxidations. The respiratory pigment cytochrome, which is said to be found in all living cells except the anaerobic bacteria, also contains iron. The daily intake with the food is about 16 mgm., and a minimum of 6 to 12 mgm. is necessary for the body to remain in iron equilibrium. The margin of safety is small. All forms of iron, whether organic or inorganic, are absorbed from the small intestine, especially in its upper part. The amount of "free iron" [1, 2] in the plasma is increased. The iron is deposited in the liver and to a less extent in other parts of the reticulo-endothelial system. The iron content of the liver may therefore be taken as a measure of absorption and of the iron stock of the body. Iron is excreted in firm organic combination through the large intestine, only negligible quantities leaving by other channels. Absorption is different from assimilation, but it is equally clear that all forms of iron can be assimilated and become an integral part of the hæmoglobin and the other tissues of the body. This is obviously true of the food iron, but it is equally true of the inorganic preparations of iron, as has been repeatedly proved by supplying iron salts to young and actively-growing animals on a diet deficient in iron, and to animals rendered anæmic by long-continued blood loss.

Animal experiments are less enlightening when we consider the therapeutics of iron. They are rather narrowly limited to the estimation of the significance of iron as a food or element of nutrition. The action of iron as a drug may not be the same as its action as a food. In animal experiments food-iron is more powerful than inorganic iron, the optimum dose of iron is small, and other mineral substances such as copper are essential. In the human anæmias in which iron is effective, inorganic iron is more powerful than food-iron, the optimum dose of iron is large, and other minerals may be disregarded under all ordinary schemes of diet. No apology is needed for considering the field of clinical medicine the real testing ground of iron therapy. All parts of this field are not equally suitable, and many cases of anæmia afford little opportunity for weighing the effect of treatment, owing to the presence of uncontrollable factors, such as a spontaneous tendency to recover, or a variation in the intensity of the anæmizing agency.

It is difficult to assess the value of treatment in anæmia resulting from hæmorrhage. Transfusion is the only remedy which has an unequivocal effect. Of seven patients with anæmia after hæmatemesis whom I have followed for three months or longer, two controls who received no hæmatinic remedies recovered just as rapidly as five who were treated with iron and ammonium citrate, 30 gr. a day; some of the latter also received liver juice. There is, however, considerable evidence that recovery from hæmorrhagic anæmia may be accelerated by iron or by liver, and that a combination of iron and liver may be more powerful than either alone [3, 4], though few of the experiments have been adequately controlled. It is unsatisfactory to test remedies on these patients, as they recover spontaneously and rapidly, and a very large number of cases and controls is necessary for the results to be significant.

Even after chronic and repeated hæmorrhage, such as may occur from hæmorrhoids and menorrhagia, recovery may occur spontaneously and rapidly when the bleeding is stopped. In a few cases the anæmia persists and shows no tendency to disappear.

Physicians a hundred years ago were familiar with persistent anæmia after excessive phlebotomy, and Graves [5], who had seen several instances of this, refers to "the account which Tacitus has so graphically drawn of the effects of loss of blood on Seneca's widow, who wishing to bleed to death with her husband, was saved by the orders of Nero, *ne glisceret invidia crudelitatis.* But the tyrant's object was not accomplished and she remained for many years, adds Tacitus, a memorial of her husband's fate, *ore ac membris in eum pallorem albentibus, ut ostentui esset.*" In such cases benefit may confidently [4] be expected from the exhibition of iron. Much the same conditions are present in hookworm anæmia, which is chiefly caused by chronic bleeding [6]. Most cases recover promptly on expulsion of the worms. Occasionally the anæmia remains torpid if not actively treated. If iron is given in such a case, there is a reticulocyte crisis and a steady rise in red cells and hæmoglobin [7].

With these few exceptions, the hæmorrhagic anæmias are unsuitable for the testing of hæmatinic remedies. Anæmia due to sepsis or cachexia is equally insusceptible of exact analysis. Another point I wish to emphasize is that no conclusions may be drawn as to the value of other remedies in a patient who has been recently transfused. The effect of transfusion in the chronic microcytic anæmias is not immediate or transient. Examination of the blood a few days after transfusion may show little change, but a steady improvement occurs for about three months. I have notes of twenty-four cases of chronic microcytic anæmia treated by transfusion. One patient died from suppression of urine [8]. The remainder all did well, though other treatment, admittedly, was used. In the first month, after an average of $1\frac{2}{3}$ transfusions, the average hæmoglobin rose from 38% to 66%. Five cases were followed through the second month; in four without further transfusion the average hæmoglobin rose from 60% to 74%; in one with two more transfusions it rose from 51% to 66%. Three cases were followed through the third month; the hæmoglobin values in these patients are as follows:—

HÆMOGLOBIN PERCENTAGE.

		Months		
	Initial	1	2	3
Mrs. H. ...	20 ...	40 ...	60 ...	80
Mrs. E. ...	30 ...	60 ...	70 ...	75
Mrs. W. ...	49 ...	63 ...	— ...	45

Although other treatment was given, and although I have no record of a patient transfused and then followed for three months without further treatment, these results are so uniformly satisfactory that we must make the provisional conclusion that improvement after transfusion may continue for at least three months, and I have therefore excluded from my analysis of the effects of iron any patient who has received a transfusion within six months.

With increasing knowledge, treatment of the anæmias is growing more accurate and better defined. Liver and stomach extracts exert a specific action on the megalocytic anæmias, thyroid extract on the anæmia of myxœdema, vitamin C on the anæmia of scurvy [9]. The hæmatinic action of iron is seen most clearly in the anæmia of prematurity, in chlorosis and in that large group of chronic microcytic anæmias which occur most typically in middle-aged women. Dr. Helen Mackay [10] has proved the value of iron in the anæmia of prematurity, a condition probably due to insufficiency of the iron reserve. My studies have been confined to adults. Obscure anæmia of the microcytic type is more common than is realized [11]. I have been able to collect a large number of cases of microcytic anæmia in patients over the age of 15, not due to hæmorrhage, sepsis or any known cause, which may be provisionally classified as follows:—

TABLE I.—OBSCURE ANÆMIA OF MICROCYTIC TYPE.

Total number of cases 111.

1.—*Chlorotic Anæmia.*

16 cases, 8 males, 8 females.
Normal test-meal.

2.—*Chronic Microcytic Anæmias of Middle and Later Life.*

95 cases, 8 males, 87 females.
Achlorhydria in 90%

(*a*) Simple achlorhydric anæmia.

75 cases, 8 males, 67 females.
Achlorhydria or extreme hypochlorhydria in all.

(*b*) Plummer-Vinson syndrome of dysphagia and anæmia.

13 cases, all females.
Test meals on 7 patients; 4 achlorhydria, 1 extreme hypochlorhydria, 1 low normal, 1 normal.

(*c*) Chronic abdominal invalidism with anæmia but normal test-meal.

7 cases, all females.

The term chlorosis is used in a broad sense [12] to include both male and female cases of anæmia of a chlorotic type, the main points being that the highest incidence is in early adult life, the test meal is normal, glossitis and dysphagia do not occur, and there is little tendency to relapse after successful treatment. The other group, which I shall refer to as the chronic microcytic anæmias of middle and later life, is characterized by a high incidence in middle-aged women, by great frequency of glossitis, achlorhydria and dysphagia, by chronicity and by a strong tendency to relapse. I cannot speak from any close experience of the microcytic anæmias of pregnancy, in spite of their importance. My impression is that the severe cases are usually associated with achlorhydria, glossitis or splenomegaly, and that they respond to iron. Strauss [13] has recently reported three cases in which achlorhydria was present, and which were cured with large doses of iron. Chlorosis and the microcytic anæmias of later life provide an ideal field for the testing of hæmatinic remedies, on account of their chronicity and the absence of disturbing factors.

Before discussing more fully the use of iron in these diseases I must briefly refer again to the use of liver. I have already quoted evidence which suggests that liver is of value in hæmorrhagic anæmia, as was to be expected from animal experiments. On the other hand I know of no evidence that either extracts of liver and stomach or whole liver have any effect in chlorosis or the chronic microcytic anæmias, and this is the conclusion of others who have studied this question [14, 15, 16, 17]. In five of my cases in which these substances were given alone for periods of from one to six months, they never produced a reticulocyte crisis, and never augmented the cells or the hæmoglobin. The two patients who had the longest treatment with liver, six weeks and six months respectively, actually deteriorated. In the present paper I hope also to disprove the belief [18] that liver, even if ineffective alone, may aid and increase the action of inorganic iron in these diseases. To assume, because liver cures the megalocytic anæmias and the anæmia of hæmorrhage, that liver must therefore be of value in other microcytic anæmias, is to make what Sir Almroth Wright has called "the generalization of ignorance," a generalization which is not supported by the facts. Indeed, the action of liver in hæmorrhagic anæmia, which is due to its content of the building stones of the hæmoglobin molecule, is quite different from its action in the megalocytic anæmias, which is due to a relatively simple substance devoid of iron, and apparently a compound of beta-hydroxyglutamic acid and hydroxyproline [19]. It is a wise measure to advise patients with chlorosis or chronic microcytic anæmia to eat not only liver, but also red meat, as their diet is often deficient in animal protein, but such a modification of the diet must not be expected to have any notable effect on the anæmia.

RESULTS OF TREATMENT IN CHRONIC MICROCYTIC ANÆMIAS OF MIDDLE AND LATER LIFE.

Note: * Starred cases have achlorhydria or extreme hypochlorhydria.

TABLE II.

Dosage of iron less than 60 grains of iron and ammonium citrate a day and no liver given.

Patient	Initial Hb.	Hæmoglobin per cent. 2 weeks	4 weeks	6 weeks	8 weeks	10 weeks	3 months	4 months	5 months	6 months
(*a*) *No hydrochloric acid.*										
Land*	35	—	40	—	42	55	—	—	—	—
Webster*	40	—	—	—	58	—	55	—	44	—
Chiverton*	32	38	51	80	—	—	—	—	85	—
Mercer*	35	—	55	—	70	—	75	80	—	—
Painter	45	53	62	55	67	—	—	—	—	—
Shepherd	47	—	48	67	55	—	—	—	—	—
Dunn	62	—	58	—	—	—	55	45	45	—
(*b*) *With hydrochloric acid.*										
Davies*	50	46	55	58	57	—	—	—	—	—

TABLE III.

Dosage of iron from 60 to 120 grains of iron and ammonium citrate a day and no liver given.

Patient	Initial Hb.	Hæmoglobin per cent. 2 weeks	4 weeks	6 weeks	8 weeks	10 weeks	3 months	4 months	5 months	6 months
(*a*) *No hydrochloric acid.*										
Edwards*	30	—	—	80	—	—	—	—	—	—
Gallagher*	33	30	40	—	—	60	—	—	75	—
Maskell*	25	—	—	48	65	—	—	75	—	—
Jackson	30	48	70	—	80	—	—	80	—	95
Painter	40	—	70	—	85	—	—	—	—	—
Smith	56	—	60	76	—	100	—	—	—	—
(*b*) *With hydrochloric acid.*										
Babbington*	32	—	—	—	52	55	60	70	—	—
Freeman*	45	—	—	—	54	—	—	—	80	—
Hind*	47	—	60	—	—	—	—	—	66	75
Cutler*	52	66	68	72	—	—	—	—	—	—

TABLE IV.

Dosage of iron and ammonium citrate 60 to 120 grains a day and liver also given.

Patient	Initial Hb.	Hæmoglobin per cent. 2 weeks	4 weeks	6 weeks	8 weeks	10 weeks	3 months	4 months	5 months	6 months
(*a*) *No hydrochloric acid*										
Edwards*	30	—	30	39	—	65	75	75	—	—
Harsant*	30	40	60	59	55	60	70	80	—	—
Davies*	61	92	—	—	—	—	—	—	—	—
Shepherd	45	—	55	—	65	—	70	75	80	85
(*b*) *With hydrochloric acid*										
Thorpe*	32	48	59	61	80	—	—	—	90	—
Freshfield*	50	—	60	69	—	—	92	—	90	—
St. Noble*	31	48	60	—	64	—	89	—	—	—

TABLE V.

Dosage of iron and ammonium citrate 200 to 350 grains a day with hydrochloric acid, but no liver given.

Patient	Initial Hb.	Hæmoglobin per cent. 2 weeks	4 weeks	6 weeks	8 weeks	10 weeks	3 months	4 months
Court*	30	42	50	61	—	80	—	98
Day*	29	35	50	48	65	—	—	—
Jarvis*	16	27	43	57	60	65	—	—

In assessing the results of the treatment of the chronic microcytic anæmias of middle and later life with iron and ammonium citrate, I have rejected all patients who had been transfused within six months and all who were not under treatment for eight weeks, unless the hæmoglobin had risen to 70% within that time. Twenty-eight cases fulfilled these conditions. The average duration of symptoms was five years and a half. In eight patients the amount of iron and ammonium citrate given was less than 60 gr. a day. Two were cured, while two had not

improved after five months' treatment; in the remainder, the length of treatment was inadequate. In seventeen patients the dose of iron and ammonium citrate was from 60 to 120 gr. a day. All were cured, the average percentage of hæmoglobin rising from 39 to 83. The increase of hæmoglobin during the first month was often small. Successful treatment required from three to four months, and some patients continued to improve for a year. As a general rule, which is liable to exceptions, the longer the history, the more refractory the anæmia. The value of persevering with treatment in spite of initial failure is shown by the following case, which is not included in the tables, as transfusions were given :—

Mrs. W., aged 45, admitted to Guy's Hospital in 1923 with a year's history of anæmia and recurrent glossitis. She was said to have had a tapeworm five months previously, but no trace of it was found. *Blood-count*, R.B.C.s 4,750,000, Hb. 48%, C.I. 0·5. Apart from the anæmia there were no other signs of disease; the test meal was normal but the Wassermann reaction was positive. A course of novarsenobillon was given but made no improvement. She was seen again 22 2 30. She had been a chronic invalid throughout, suffering from anæmia, occasional soreness of the tongue, and dyspepsia with alternating constipation and diarrhœa. There were no signs of organic disease in the alimentary canal, the fæces were normal and the test meal showed brief hyperchlorhydria. *Blood-count*, R.B.C.s 3,280,000, W.B.C.s 12,700, Hb. 25%, C.I. 0·4. The Wassermann reaction was now negative. She was treated with iron, liver and transfusions, and left hospital in May with 63% hæmoglobin. Much of the improvement must have been due to the transfusions, for in spite of 75 gr. of iron and ammonium citrate a day, the hæmoglobin had fallen a month later to 40%. The iron was increased to 90 gr. and later to 120 gr., and from this point there was a steady improvement, as shown by the hæmoglobin percentages in the successive months :— June 40%, July 45%, August 55%, October 80%, November 95%.

No uncomplicated case has failed to respond to treatment with iron and ammonium citrate, when the drug was given in adequate amounts and for sufficient time. My only failure has been in a Plummer-Vinson syndrome, complicated by almost daily attacks of purpura, apparently due to an infected nasal sinus for which the patient refuses operation. Under treatment with 90 gr. of iron and ammonium citrate a day, her hæmoglobin rose in four months from 35% to 58%, but I cannot get it higher. Failure in treatment should suggest a wrong diagnosis or a complication.

Although the effective dose of iron and ammonium citrate must be placed at not less than 60 gr. a day, there is no advantage in giving doses very much greater than this. The mean duration of treatment is not shortened. One of our patients was given 240 gr. of iron and ammonium citrate a day and two others 350 gr., but they did not do better than the others. One can therefore say that the dose of iron and ammonium citrate in the chronic microcytic anæmias should be from 60 to 120 gr. a day, that the treatment must be expected to take at least three months, that the rise in hæmoglobin in the first month may be very small, and that in spite of the initial delay treatment is practically always successful.

The lag in response to iron, and the tendency for the hæmoglobin to rise much more steeply in the second than in the first month, must caution us from drawing unjustifiable conclusions from the successive exhibition or intercalation of different remedies, or the addition of other forms of medication. The view that liver, while ineffective alone, supplements and increases the action of iron in the microcytic anæmias, is founded on fallacious experiments of this kind. In the tables, I have separated the patients who had iron alone from those who had liver also. In 10 who had adequate iron but no liver, the average hæmoglobin rose from 39% to 80%; in seven who had adequate iron plus liver, it rose from 40% to 86%. There was therefore no real difference in the increase of hæmoglobin and the mean duration of treatment was the same in the two groups.

Nor is there any evidence that when achlorhydria or hypochlorhydria is present,

the anæmia responds better if acid also is given. In six achlorhydric patients treated with adequate amounts of iron alone, the average hæmoglobin rose from 35% to 80%; in seven who had in addition amounts of dilute hydrochloric acid, from 90 to 480 minims a day, the average hæmoglobin rose from 41% to 77%. Again, the increase of hæmoglobin and the duration of treatment were identical. We must therefore conclude that the action of iron is not assisted by either liver or hydrochloric acid. This conclusion must be qualified by a reference to the work of Mettier and Minot [20], who were able to induce a reticulocyte crisis and accelerate the recovery of patients with achlorhydria and anæmia, who were being treated with small doses of iron, by administering hydrochloric acid as well. A further reticulocyte crisis and acceleration of recovery could afterwards be obtained by quadrupling the dose of iron. In patients with achlorhydria and anæmia then, although the absorption of a sub-optimal dose of iron is promoted by giving hydrochloric acid, the therapeutic action of iron is most surely obtained by administering large amounts of iron, when the effect of the acid becomes negligible.

The tendency of the chronic microcytic anæmias of middle and later life is to relapse, either immediately after ceasing treatment or at an interval of months or years. I recently followed up 22 patients, who had been treated two or more years before, and found that only four had remained well. Where there are no facilities for regular blood-counts, and that is in the majority, the patient should continue to take iron indefinitely. The hæmoglobin can usually be maintained at a satisfactory level by a daily dose of 20 gr. of iron and ammonium citrate or 10 gr. of Blaud's pill. It is not sufficient to advise the patient to resume iron when symptoms recur, as many have no symptoms till the hæmoglobin falls below 40%, and they will then not respond to such a small dose.

The results of treatment in cholorosis can be reviewed more summarily. Most of the cases in the following table received large doses of iron and ammonium citrate, but chlorosis will sometimes respond to a smaller dose of iron than the chronic microcytic anæmias of later life. The duration of treatment is shorter, an average case being cured in six weeks. Relapse is uncommon and it is usually not necessary to prescribe a maintenance dose of iron. Before discussing more general aspects of the therapeutics of iron, I must emphasize that these effects of iron are confined to the microcytic anæmias, whether secondary to some known cause, or of obscure origin. Iron alone has no action on the megalocytic anæmias or on aplastic anæmia. I am informed by Dr. Janet Vaughan and Dr. T. Izod Bennett (personal communications) that in cases of Addison's anæmia, in which a normal blood-count has not been obtained on treatment with liver, complete recovery may sometimes be brought about by the addition of iron.

TABLE VI.

Results of treatment in chlorosis.

		Hæmoglobin per cent.					
Patient	Initial Hb.	2 weeks	4 weeks	6 weeks	8 weeks	10 weeks	12 weeks
Harper	60	80	—	—	—	—	—
Phillips	46	60	69	—	—	—	—
Campbell	29	40	75	—	—	—	—
Fleetwood	38	50	70	—	85	—	—
Hastings	34	39	56	73	—	—	—
Cronin	35	—	—	—	68	—	75
Bartlett	50	—	65	75	—	—	—

Iron has long had a reputation as an emmenagogue and an ecbolic. In the anæmias with which I have been dealing, amenorrhœa and menorrhagia are equally common. It is not unusual for the periods, which were scanty when the hæmoglobin was low, to become excessive when the hæmoglobin is raised above 75%. This is indeed a frequent and troublesome complication of treatment. If treatment is omitted and the hæmoglobin falls below 50%, relative amenorrhœa again appears.

In some cases I have discontinued iron during the period and the days shortly before and after, replacing it by 90 gr. of calcium lactate, but I have never been able to satisfy myself that this did good. Indeed it is not so much the iron as the improvement in the blood which is responsible for the menorrhagia. Fortunately the menstrual function usually becomes normal after a few months if the patient rests in bed at the periods. If menorrhagia persists in a middle-aged woman, subtotal hysterectomy, or sterilization by X-rays or radium is advisable. Kaznelson and others [21] have found that, far from aggravating hæmorrhage, iron acts almost specifically in arresting juvenile menorrhagia, nose-bleeding, and other manifestations of a hæmorrhagic tendency.

I have already discussed the average speed of hæmoglobin regeneration with iron. I have not made any estimations of the blood-volume, but there is general agreement that this is diminished in all forms of anæmia, so that the improvement is greater than appears from the ordinary blood-count. When the red cells are diminished to three millions or less, there is a reticulocyte crisis of from 5% to 10% in the fortnight after beginning treatment. A transient polycythæmia may occur later, the red cells reaching six millions, while the hæmoglobin is only about 70%. In other cases the number of red cells may have been normal from the start, the anæmia being essentially a hæmoglobin deficiency; improvement is then marked by a steady rise in hæmoglobin and colour index, without change in the number of red cells.

I must next speak of the mode of administration of iron and the relative activity of the different preparations. All the effects of iron can be produced in experimental animals by the injection of double salts, such as the tartrate of iron and sodium, which do not coagulate the blood and at the same time are capable of freeing the ferrum ion in the tissues. With large doses there is true iron poisoning, characterized by progressive paralysis of the central nervous system, accompanied by weak convulsive movements, vomiting and diarrhœa. Chlorosis has been cured by injection of iron. The daily injection of 1 to 2 gr. of neutral iron and ammonium citrate in 5% or 10% solution is recommended in human cases, but the injections are extremely painful, and gastro-intestinal disturbances may still be produced by the iron, which is excreted through the alimentary tract [22]. If iron is not tolerated by mouth, the obvious remedy is transfusion. The present fashion of injecting unofficial preparations which contain infinitesimal amounts of iron cannot be too strongly criticized. I have carefully observed patients treated with injections of colloidal iron, iron cacodylate, ferrarin, Fraisse's serum and similar preparations, and the results have been uniformly bad.

The value of large doses of iron by mouth seems first to have been appreciated by Lichtenstein [23], who gave 0·5 grm. of ferrous lactate three times a day to infants prematurely born. In adult cases, especially simple achlorhydric anæmia, their value has been emphasized by Meulengracht [24], who found the optimal dose of reduced iron to be from 0·5 to 1·0 grm. three times a day. He increased the dose for the sake of curiosity to 10 grm. a day; the larger dose offered no special inconvenience, but, on the other hand, no advantage. In this paper I have reported cases tolerating over 20 grm. (350 gr.) of iron and ammonium citrate a day without symptoms. There is no recorded instance of poisoning from iron administered medicinally. There are several cases of poisoning by ferrous sulphate and by tincture of ferric chloride, usually in the attempt to procure abortion, but the symptoms were those of gastro-intestinal irritation and were due to the local action on the alimentary canal of enormous doses in concentrated solution. I have yet to meet a patient who cannot take iron, though I have met one who would not. This was a nurse who had overheard the physician say that iron did not suit her, as she was slow in improving. One of Dr. Hurst's patients, a chronic abdominal invalid, complained of pain after iron and ammonium citrate,

but was able to take a mixture of 3 drachms of tincture of ferric chloride in 1½ oz. of chloroform water four times a day. Large doses of iron and ammonium citrate after meals do not produce constipation and their effect on the digestive system is often strikingly beneficial. Intolerance to iron is usually due to suggestion and it is rarely met by the physician who is fully conscious of the harmlessness of large doses of iron.

Starkenstein [25] has pointed out that there are over 600 preparations of iron at the disposal of the physician, and has suggested the following classification :—

(1) Simple inorganic ferrous salts, e.g., ferrous chloride, ferrous sulphate, ferrous lactate : metallic iron is included here, as it is converted into ferrous chloride in the stomach.

(2) Simple inorganic ferric salts, e.g., ferric chloride, saccharated iron, albuminate of iron.

(3) Complex inorganic compounds, such as iron and ammonium citrate and iron and potassium tartrate.

(4) Organic compounds of iron, such as hæmoglobin, in which the iron is "masked."

In animal experiments Starkenstein found that only the ferrous salts and the complex double salts were pharmacologically active; ferric salts and organic compounds of iron were inactive. Working on Starkenstein's suggestion, the Prague school of hæmatologists has found that ferrous iron is a much more powerful remedy than any other preparation. I have treated only a few cases with ferrous salts, but the results confirm these findings. Of the following cases of simple achlorhydric anæmia, two were treated with a daily dose of 30 gr. of Blaud's pill, one with 45 gr. and the fourth with 7 gr. of ferrous chloride (9 tablets of ferronyl). All did well and the treatment was shortened from the usual three or four months to six or eight weeks. Another of my patients, who had not improved after five months' continuous treatment, with 30 gr. of iron and ammonium citrate a day, was treated by another physician with 30 gr. of Blaud's pill daily, and when I saw her again her hæmoglobin had risen from 45% to 70%.

TABLE VII.

Results of treatment of simple achlorhydric anæmia with ferrous salts. equivalent 0·2 to 0·3 grams of iron a day.

		Hæmoglobin per cent.				
Patient	Initial Hb.	2 weeks	4 weeks	6 weeks	8 weeks	10 weeks
Cartwell*	50	—	55	—	—	75
Marshall*	28	26	46	70	—	—
Evans*	32	42	48	64	75	—
Pritchard*	46	50	70	—	—	—

Reimann [26] has compared the activity of the various preparations of iron by giving them in a dose equivalent to 0·1 grm. of iron a day. Ferrous iron was the only form which produced improvement in this dosage. In the following table I have compared the minimum effective dose of different forms of iron, working out their iron equivalents. This leaves no doubt about the superiority of ferrous iron. The inactivity of metallic iron is due to its insolubility. It acts better in chlorosis, where the gastric secretion is normal, than in simple achlorhydric anæmia. The ferrous salts of iron are active in smaller dosage and produce a more rapid effect than any other preparations of iron.

TABLE VIII.

Minimum effective dose and iron content in grams of different preparations of iron.

Preparation	Authority	Minimum effective dose in grams	Iron content	Valency
Reduced iron	Meulengracht	1·5 to 3·0	1·2 to 2·4	Metallic
Idozan (Ferric hydroxide)	Meulengracht	30·0 to 45·0	1·5 to 2·25	Ferric
Iron and am. citrate	Witts	4·0 to 8·0	0·8 to 1·6	Ferric
Pil. ferri	Witts	2·0 to 3·0	0·2 to 0·3	Ferrous
Ferrous chloride	Reimann	—	0·1	Ferrous

I have discussed the therapeutics of iron from an empirical standpoint. Iron therapeutics originated in sympathetic magic. The weakly sufferer, who drank the water in which a sword had rusted, or in which the smith had quenched the glowing metal, did so in the hope of imbibing something of the strength of steel. We are still ignorant of the causes of chlorosis and the chronic microcytic anæmias of later life. There is a feeling that they are due to iron deficiency, but there is little convincing evidence. We await careful studies of the iron intake in health and disease, of the effect of the hydrogen-ion concentration of the alimentary tract on the absorption of iron [27], of the free iron of the plasma and the iron of the tissues, and of the whole iron balance of the organism. It remains obscure why different forms of iron should be absorbed equally well and yet differ greatly in pharmacological action. The time is not ripe for theoretical discussion of the therapeutics of iron, and I will close with a few empirical conclusions:—

(1) The action of iron in human anæmias may be different from its action in the experimental anæmias of animals.

(2) Anæmia due to hæmorrhage, infection, or cachexia is rarely suitable for therapeutic trials; the same is true of cases recently transfused. Chlorosis and the chronic microcytic anæmias of later life form an ideal testing ground of iron therapy.

(3) The minimum effective daily doses of the different preparations of iron are: Reduced iron 25 gr. (1·5 to 3·0 grm.); Blaud's pill, 30 gr. (2·0 to 3·0 grm.); ferrous chloride, 4gr. (0·25 grm.); iron and ammonium citrate, 60 gr. (4·0 to 8·0 grm.). Very much larger doses can be given without ill effect—but also without advantage.

(4) Large doses of iron improve digestion, and intolerance is rare.

(5) Iron should not be given by injection, owing to the long duration of treatment and the difficulty of giving adequate doses by this route.

(6) Cure of a severe anæmia takes three or four months, and the improvement in the first month may be small. The longer the duration of symptoms the longer is the treatment necessary.

(7) The maintenance dose of iron is not more than one-third of the minimum effective curative dose.

(8) Chlorosis responds to iron more readily than the chronic microcytic anæmias of later life, and less often relapses.

(9) Liver has an adjuvant effect on the action of iron in hæmorrhagic anæmia, but not in chlorosis, or the chronic microcytic anæmias. In cases of achlorhydria, hydrochloric acid promotes the absorption of small doses of iron, but with adequate dosage of iron the effect of the acid is not appreciable.

(10) Menorrhagia not infrequently occurs in women when an anæmia has been successfully treated with iron. It is not clear whether it is due to the iron or to the improved blood supply. Iron is stated to have a specific action in checking juvenile menorrhagia.

(11) The preparations of iron may be classified into the ferrous salts, the scale preparations, metallic iron, the ferric salts and organic iron, and this is also the order of their efficiency. The ferrous salts act in a smaller dosage and in a shorter time than the other preparations.

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Dr. Daniel T. Davies said that he had obtained uniformly good results with iron therapy in cases of secondary anæmia with achlorhydria. The preparation used was iron and ammonium citrate and the dose from 60 to 80 gr. a day. No case of intolerance had been encountered and many of the patients experienced a lessening in abdominal discomfort with improvement in the blood. Since the beneficial results were so constant, it appeared quite unnecessary to entertain any other than the oral method of administration. It was noted that in addition to an improvement in the blood, which was observable within a month in the majority, the previously enlarged spleen receded behind the costal margin, the tongue showed less glossy changes, and the nails, previously brittle and painful, became more normal. [Details of such a case of anæmia following a gastro-enterostomy were given, and photographs of the nails showed the spoon-shaped form being replaced by the normal type, three months after the commencement of iron therapy.]

Although achlorhydria was a usual finding, this was not such a constant feature as in pernicious anæmia. As ferments were still being secreted, it could not be regarded as an achylia. The increased viscosity of the gastric juice was a finding suggestive of gastritis and was in keeping with the constant gastric symptoms of these patients. The observations of Mettier and Minot, quoted by Dr. Witts, on the repeated reticulocytosis produced by changing the reaction of the stomach juice while iron was given, suggested that the achlorhydria played an important part in the development of the anæmia. The best example of a constant gastric reaction—free of acid secretion—was, however, that found in pernicious anæmia—a disease in which there was no lack of iron.

All the patients studied had for years existed on a poor protein diet, and it was found that the majority of the women seldom ate any meat. A similar defective diet was present in those cases of Plummer-Vinsen syndrome. The abnormal diet and the gastritis were important factors in elucidating the cause of the anæmia—possibly resulting in a deficient intake or absorption of iron. The immediate improvement following iron administration suggested that the other departures, such as in the tongue mucosa, in the character of the nails, and the splenic enlargement, were secondary to the anæmia consequent on an iron deficiency. Further studies on this common disability of middle-aged women might demonstrate the alimentary origin of yet another anæmia. The character of the gastric secretion in anæmia might prove to be of some importance, since persons with a potent gastric juice seemed to recover a normal level more rapidly after a blood loss than those with a poor gastric secretion, irrespective of any treatment.

Dr. Helen M. M. Mackay: My contribution to this discussion is confined to the effects of iron therapy on infants and young children. It is based on work done during the past five years by Miss Lorel Goodfellow and myself, part of which I described at a meeting of the Section for the Study of Disease in Children about two years ago.[1] Although the work was mainly done in the out-patient department of the Queen's Hospital for Children, the babies whom we treated prophylactically were mostly not sick children, but infants of the type found in welfare centres; hence I believe our results will be found to apply to infants in general, and should not be regarded as applying only to sick babies.

THE EFFECTS OF IRON THERAPY ON ARTIFICIALLY-FED BABIES.

Iron and ammonium citrate was the salt used in nearly all our work. It can easily be given to infants, provided a few precautions are observed.

[1] *Proceedings*, 1929, xxii, 385 (Sect. Dis. in Child., 29).

There are three main effects to which I would like to draw attention: (1) the effect on the hæmoglobin level; (2) the effect on the morbidity rate; and (3) the effect on the weight.

Effect on the hæmoglobin level.—Iron raised the hæmoglobin level of the great majority of infants treated. Chart I shows the hæmoglobin level of groups of artificially fed infants beginning treatment at different ages, compared with a corresponding control group of untreated infants. Each group treated with iron had at the outset an average hæmoglobin level near, or below, that of the controls at the

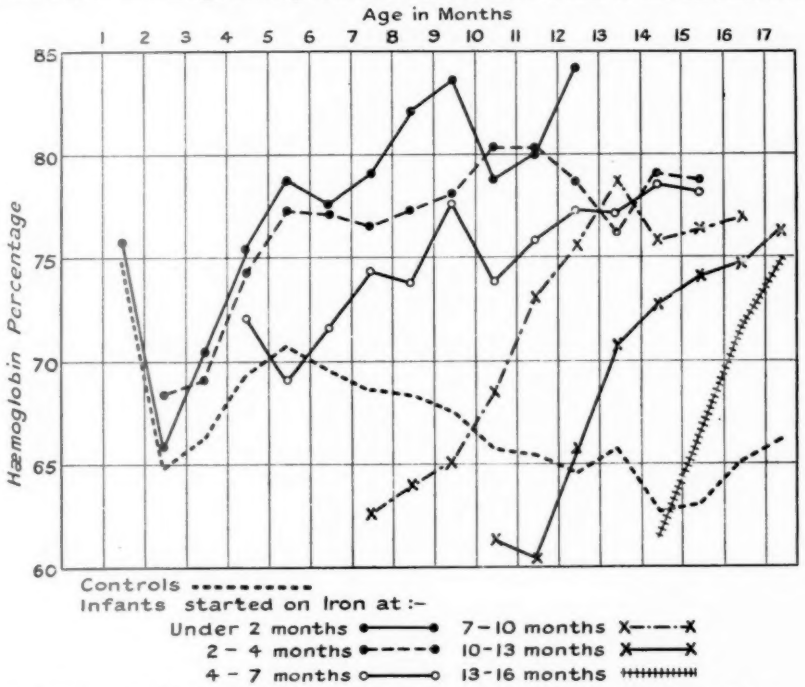


CHART I.—*The Effect of Iron Treatment on the Hæmoglobin Level of Artificially-fed Babies.* Babies grouped by age of starting iron.

Number of Estimations on which Chart I is Based.

Months of Age	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Infants starting iron at																	
Under 2 months old ...	22	16	19	17	15	15	14	11	7	10	8	5					
2 to 4 ,, ,, ...	...	29	48	41	44	39	36	33	30	24	18	9	12	13	4		
4 to 7 ,, ,, ...	...	...	...	17	19	29	28	24	21	21	19	18	14	9	5		
7 to 10 ,, ,, ...	...	...	...	...	...	...	7	16	25	22	17	15	10	8	7	6	
10 to 13 ,, ,, ...	...	...	...	...	...	...	...	...	...	6	11	20	16	12	9	8	5
13 to 16 ,, ,, ...	...	...	...	...	...	...	...	...	...	...	...	...	...	8	11	9	7
Controls	42	99	111	114	116	113	115	100	85	74	66	58	35	38	33	28	19

same age, but with iron there was a fairly steady rise in hæmoglobin, in spite of the fact that in many cases iron administration was irregular, and that cases inadequately treated pulled down the averages. These infants were not babies selected for anæmia, so that the hæmoglobin level of the controls represents, I think, a fair average level for artificially-fed babies. It was approximately the same as that obtained at a welfare centre in Lambeth, where the general level of health was otherwise good. A comparison of treated and untreated cases, therefore, compels the conclusion that the infants in our control series were, for the most part, anæmic.

The infants of whom I have been speaking were artificially fed, but our work in the infant welfare department of the Mothers' Hospital, Clapton, showed that anæmia was also extremely common among breast-fed babies. In a special group of breast-fed babies who had not suffered from any illness, the hæmoglobin level was only about 4% higher than in our control group of bottle-fed babies. This group was carefully selected to exclude all infants of poor physique; all the babies included weighed over 6 lb. at birth, and showed good growth, and any baby who was known to have suffered from any illness, even a cold in the head, was excluded. From this we conclude that this form of anæmia was not, for the most part, secondary to

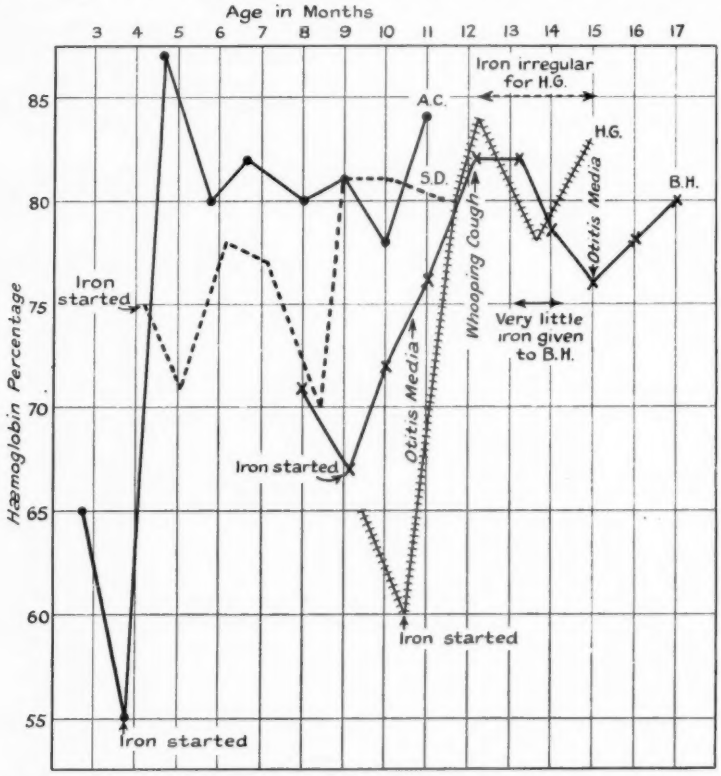


CHART II.—*Individual Hæmoglobin Curves. The Response to Iron Treatment in Four Artificially-fed Babies.*

disease. Nor can it be attributed, in face of the facts available, to one particular method of infant feeding. There is, on the other hand, a great deal of evidence to show that it is the result of iron deficiency, and that this deficiency is most marked in babies who are small at birth, and who, relative to their initial weight, increase in size rapidly.

The effect of iron therapy on individual anæmic babies is shown in charts II and III.

The first shows the hæmoglobin curves of four artificially-fed babies starting iron treatment at ages varying from four to ten months; three of these show an immediate and satisfactory response, with a rise in hæmoglobin to about 80%, which

we consider normal at these ages; the fourth gave a poor response, though ultimately the hæmoglobin reached 80%.

The next chart is of three premature infants: two of them, who were treated from the second month of life, show a satisfactory hæmoglobin level; the third shows a typical curve for an untreated infant up to nine months of age when the

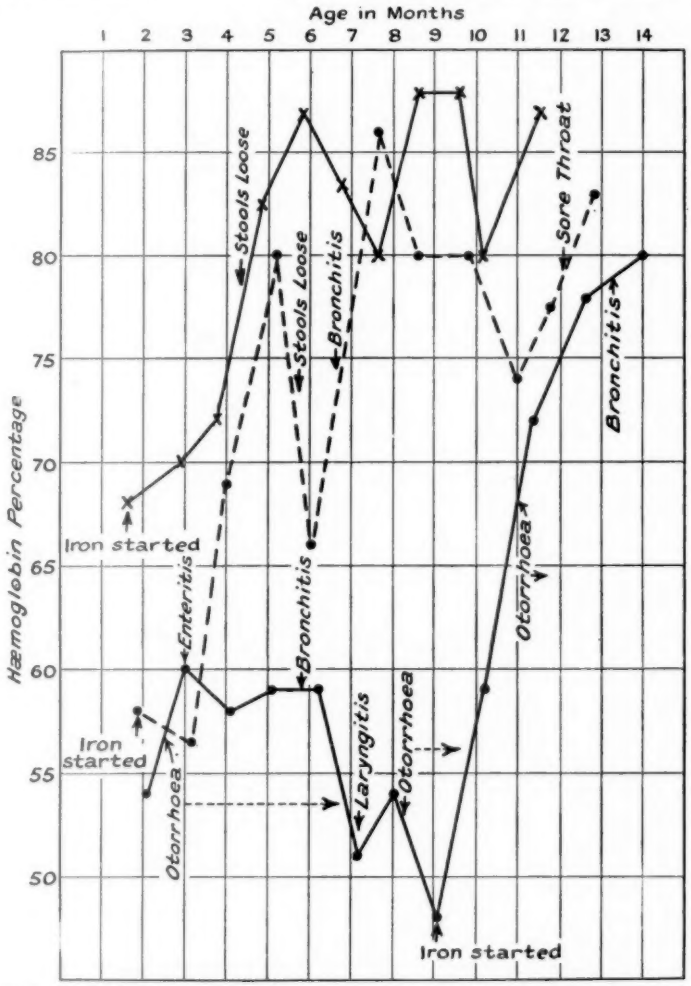


CHART III.—*Individual Hæmoglobin Curves. Premature Infants.* (Birth-weight 3 lb. to 4¾ lb.) *Effect of Iron Treatment* from 2 months old and from 9 months old.

hæmoglobin was 48%; iron was then given and the hæmoglobin rose steadily till it reached 80%.

I should like here to point out a trap which has to be avoided when considering the effect of a therapeutic agent on the hæmoglobin level in infancy. It is this. After about two or three months of age nearly all infants exhibit a spontaneous,

though temporary, rise in hæmoglobin. Both the age at which this rise occurs and its magnitude vary in different individuals; it may be only a rise of 5%, or it may amount to 25% or even more (Chart IV). Hence great caution must be used in drawing conclusions as to the effects of any form of therapy on the hæmoglobin level

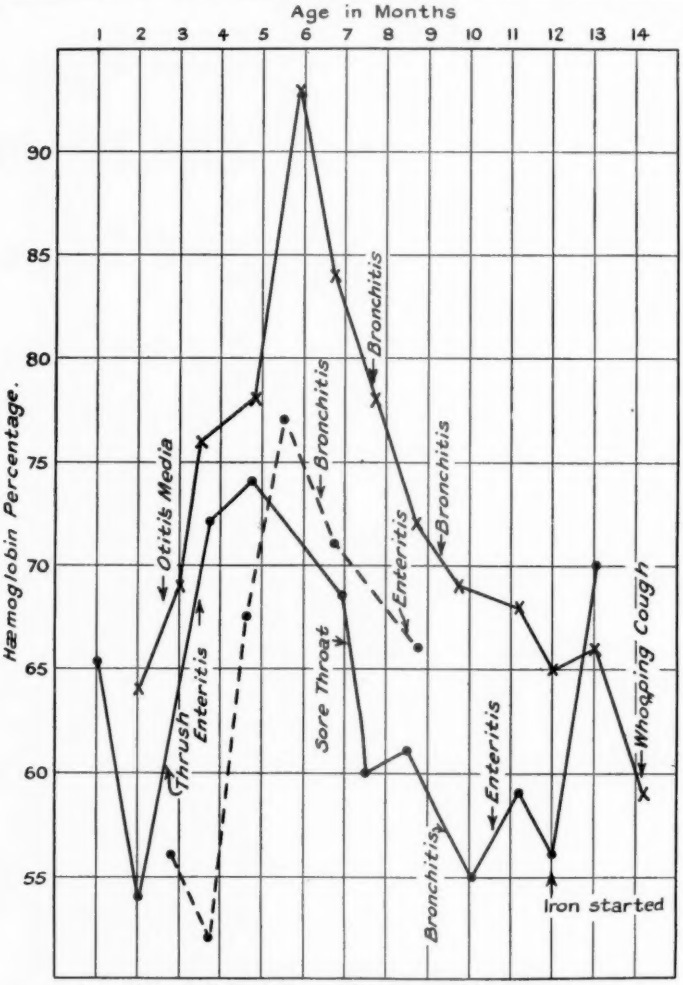


CHART IV.—*Individual Hæmoglobin Curves. Untreated Infants.*
Three full-term artificially-fed infants showing especially large rises in hæmoglobin level in the second quarter of the first year of life, and a subsequent fall.

of infants from, say, two to seven months of age, unless the numbers of treated cases and of controls are such as to place the matter beyond doubt.

Effect on the morbidity rate.—Now though the effect of iron therapy on the hæmoglobin level in infancy is striking, we have evidence of a much more remarkable result, though very possibly this may be secondary to the influence on hæmoglobin building.

By iron therapy we have approximately halved the average morbidity rate in a large group of babies treated in their own homes during the last two years. The following table shows that whether we consider all diseases, or diseases of the respiratory tract and gastro-intestinal tract separately, iron therapy has lessened

MORBIDITY RATES.

Comparison of Iron Cases and Controls (1928-1929).

	CONTROLS.			IRON CASES.		
Number of infants	66			56		
Average no. of months' observation per infant ...	4·7			6·6		
Disease	Number of attacks	Number of attacks per 100 cases per month		Number of attacks	Number of attacks per 100 cases per month	Ditto, expressed as percentage of attacks in controls
Respiratory tract—						
Cold in head, sore throat, etc.	40	12·9	29·3	29	7·8	60
Bronchitis	36	11·6		23	6·2	53
Pneumonia	4	1·3		0	0	0
Otorrhœa	11	3·5		6	1·6	46
					15·7	54%
Digestive tract—						
Stomatitis	0	0	10·6	3	0·87	0
Diarrhœa or vomiting ...	33	10·6		16	4·3	41
					5·1	48%
Specific infectious fevers ...	2	0·6		1	0·3	50%
Other diseases	3	1·0		1	0·3	30%
Total ...	129	41·5		79	21·4	52%

the illness rate by about half. We had indications of this before, but owing to seasonal variation, our controls were open to criticism, hence the work was repeated. Both in winter and in summer and at every age (Chart V), the infants having iron treatment have a much lower morbidity rate. By formulating certain rules, the illness-count was rendered as objective as possible. We are much indebted to Dr. Bradford Hill for his statistical investigation and confirmation of our conclusions on this point. I believe we can, therefore, safely claim that systematic iron therapy would decrease the general infant morbidity rate to a remarkable extent.

Effect on growth.—The third effect of iron therapy in infancy to which I want to draw attention is improved growth. This is probably in large part due to fewer infections resulting from the improved resistance, but may in some cases indicate that iron deficiency had been a direct limiting factor in growth.

Chart VI gives the average weight-curves for both treated and untreated groups of artificially-fed babies. This comparison shows that the iron cases at 4 to 6 months old were about ¾ lb. heavier, at 7 months 1 lb. heavier, and from 8 to 11 months, at least, 1¼ lb. heavier than the corresponding controls. The chart, however, does not fully indicate the superiority of the iron cases, since each curve does not represent the weights of babies remaining continuously under observation from 2 to 13 months old, for new cases were being included at most ages, and at every age old ones were dropping out. Dr. Bradford Hill accordingly tackled the problem rather differently, and his statistical examination shows that at the ages when, by our theory, iron deficiency would be most likely to be present, the difference in weight between iron cases and controls amounted to as much as 2 to 2½ lb. in babies who had had three months of treatment.

IRON DEFICIENCY IN INFANCY AND THE PART PLAYED BY COPPER IN THE CURE OF ANÆMIA.

The theory that this so-called "simple" anæmia of infancy is due to iron deficiency is, of course, based on Bunge's work carried out thirty to forty years ago. He showed that young animals are dependent during the period of exclusive milk

feeding, on the iron stored in the liver at birth, as the iron content of milk is very low. It seems from our results that in some babies, especially rapidly growing babies who were small at birth, the liver store is proving inadequate as young as 3 months of age; in babies large at birth, rate of growth relative to birth-weight is likely to be slower, and the iron store may last out much longer.

No doubt many of you have wondered how far our results were due to iron

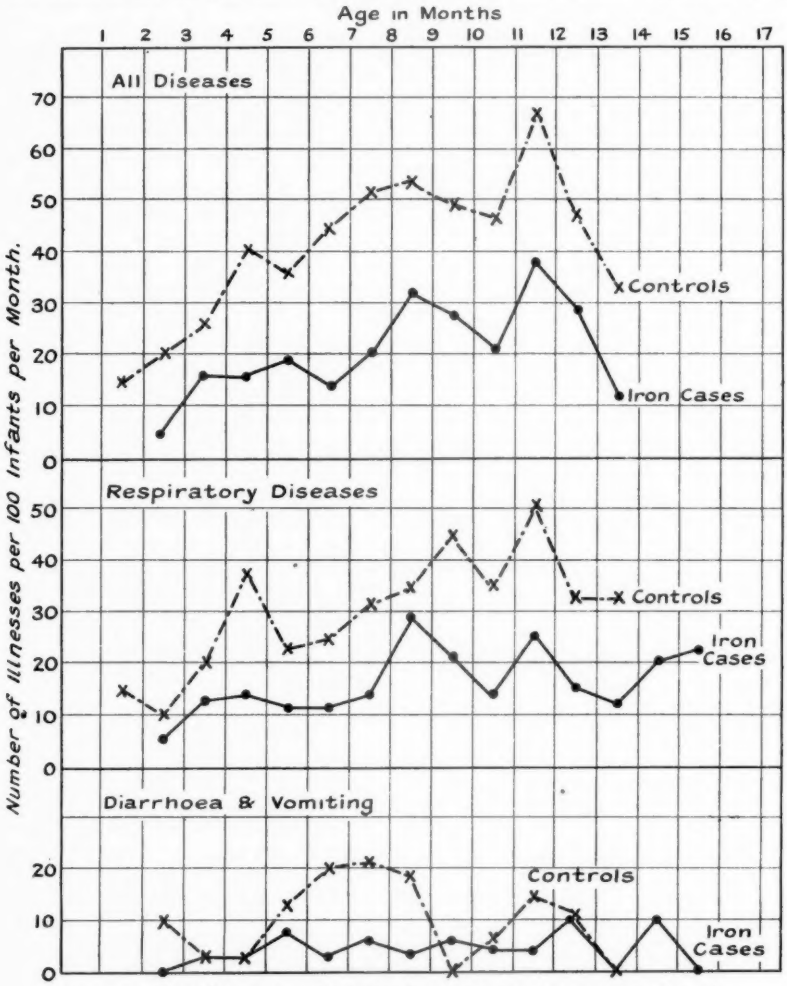

Age in Months
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17
All Diseases
Controls
Iron Cases
Respiratory Diseases
Controls
Iron Cases
Diarrhoea & Vomiting
Controls
Iron Cases
Number of Illnesses per 100 Infants per Month.
0 10 20 30 40 50 60 70

CHART V.—*Morbidity Rate at Each Month of Age in Iron Cases and in Controls.*
(Artificially-fed infants.)

therapy, pure and simple, and how far to any impurities contained in the iron salt. On this point I can give no final answer. The iron and ammonium citrate we used contained traces of both copper and manganese. Professor Hart of the University of Wisconsin was kind enough to estimate the copper content. It was such that the daily copper intake of a baby of say 10 lb. weight was only raised about 4% by

the administration of the iron salt, so that it is open to question whether this small amount of copper played any significant part in preventing and curing anæmia. On account of individual variations in response to treatment, comparatively large numbers of babies are necessary to establish the superiority of one method of treatment over another; hence to determine whether a larger copper addition would give improved results is not as simple as it might seem, and the production of a scale preparation of iron absolutely free from copper appears to be a matter of much technical difficulty.

Iron and ammonium citrate is well tolerated even by very young infants of

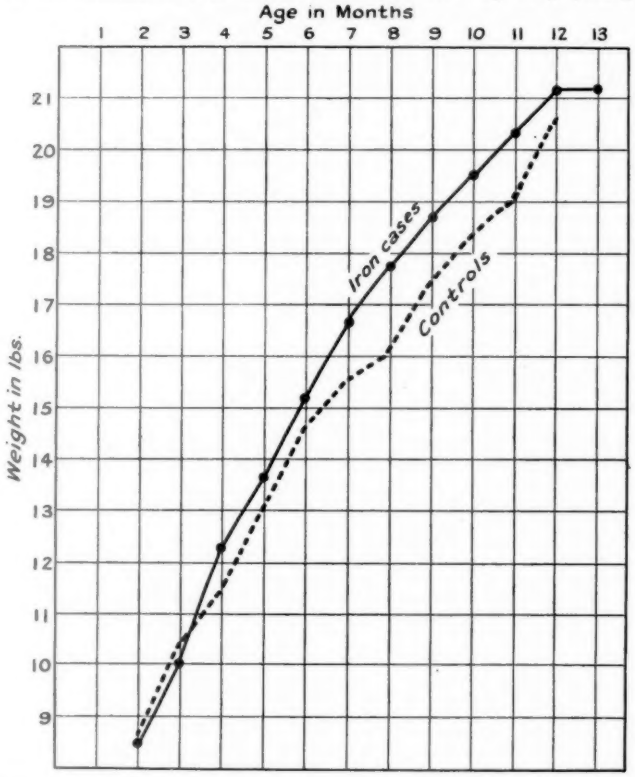


CHART VI.—*Weight at each Month of Age. Comparison of Iron Cases and Controls.* (Artificially-fed infants.)

normal digestive power, provided it is begun gradually. If not begun gradually it is likely to cause colic and diarrhœa. My plan of treatment has been to give the iron to bottle-fed babies in the feeds, either in the form of a mixture or incorporated in the milk before drying. The "Cow and Gate" firm have now on the market a dried milk, "Hemolac," containing the same quantity of iron as that used in our work, and obviously to give such a milk ensures regular administration. If, however, a baby is to be put on to such a milk, this should be incorporated gradually in the previous feed, taking perhaps a week to complete the change over, longer if the baby's digestive powers are weak. If the drug is given in the form of a mixture, gradual training to the full dose is equally necessary.

A healthy baby of, say, four weeks and upwards can usually be trained to take 4½ grains daily; older infants of four months and upwards will learn to take two or three times this amount. Dr. Witts has pointed out the advantage of large over small doses of iron and ammonium citrate in the treatment of anæmia in the adult. It is interesting to note that the doses I have been giving to infants are also large in relation to body weight. The problem of why such doses are advantageous still awaits solution, but it may be that the impurities in the salt are of fundamental importance.

[*The data on which the above statements are based will be published in full in one of the Medical Research Council's Special Report Series.*]

Dr. Janet Vaughan said she would like to ask Dr. Mackay whether the weight-gain found in children taking iron was associated with an increased food intake. This weight-gain parallelled that reported as occurring in cases of pernicious anæmia receiving liver therapy and which she had only found in patients whose food intake was unlimited. Patients on a basal calory diet showed no increase in weight, suggesting that increased caloric intake was the important factor.

She did not agree with Dr. Witts' conclusion that iron was of no value in the treatment of pernicious anæmia. She had seen cases in Dr. Minot's clinic in which the blood-count remained at levels in the region of 3,500,000 red blood-cells per c.mm., in spite of liver therapy, but, on the addition of iron, reached a satisfactory level.

Dr. Bradford Hill said: I have had the privilege of making a statistical analysis of the material that Dr. Mackay has discussed this evening. Like all statisticians I am profoundly sceptical of other people's figures, and the difference in morbidity rates that Dr. Mackay has shown you between her "iron" group and her "control" group, at first made me suspicious that some form of selection had played a part. By selection I do not mean an error or bias in the way in which the infants were originally distributed to the two groups, but there are forms of selection which no one but the laboratory worker can keep under control. Dr. Mackay was not in a position to compel attendance at the hospital or clinic, and a mother ceased to bring her child or not as she wished. Actually it was found that infants having the iron salt attended for a longer period than the control babies, and this suggested that there might be selection in the following form: control babies came for advice and treatment; if they were doing well the mothers might cease troubling to attend; if they were doing badly they would continue to attend, i.e., those suffering most illness would attend the longest; babies on dried milk containing iron could not obtain the same food elsewhere; therefore their mothers had an incentive to bring them apart from health reasons, and there would not be so strong a tendency for the weaker babies to attend for the longest period. This possible selective force, and others, we tested by statistical methods, but in each case we reached the same answer—the "iron" group suffered only half the sickness rate of the control group, and there seems little doubt that this difference is a true one, and is not due to selection.

Another point of some interest, and one that needed statistical treatment, was the relationship between the three factors, hæmoglobin level at any time in the first year of life, birth weight, and rate of growth. If hæmoglobin level was low, was this due to a low initial birth weight, or was the birth weight immaterial and a rapid rate of growth over the first few months of life the important factor? Birth weight and rate of growth were themselves so highly correlated that the relationship of each separately to hæmoglobin level was at first sight obscure. The analysis that we made showed that, to begin with, birth weight and hæmoglobin level were related one to another to a slight extent, but by 6 months of age the birth weight was immaterial and the past rate of growth was the dominant factor. If the rate of growth had been rapid the hæmoglobin level tended to be low, if the rate of growth had been slow the hæmoglobin level tended to be high.

Section for the Study of Disease in Children.

[*November* 28, 1930, *continued.*]

Congenital Dilatation of Ureter.—B. B. HOSFORD, M.D. (for HUGH THURSFIELD, M.D.).

L. S., female, aged 3 years, child of healthy parents, has from age of 3 months been subject to attacks of fever accompanied by passage of thick, muddy urine. These have occurred at three-monthly intervals and lasted for from three days to a week. Recently urine has been continuously turbid and child has complained of abdominal pain.

Present appearance.—Fairly healthy; slight puffiness of face. Abdomen: normal. Urine turbid and contains blood and pus. Cultures show *Bacillus coli* and *Staphylococcus albus*. Blood urea: 40 mgm. %.

Cystoscopy.—No obstruction or abnormality of urethra; bladder showed marked cystitis, but no abnormal dilatation and no diverticula. Ureteric orifices appeared normal.

Catheterization of ureters, May, 1930.—Turbid urine obtained from both sides, and both specimens, on culture, showed *B. coli*.

Radiographic examination: On the left side the catheter had coiled up on itself inside a much dilated ureter.

Pyelography.—Right side: normal renal pelvis with slightly dilated ureter (fig. 1, p. 20). Left side: slightly dilated renal pelvis with enormously dilated and tortuous ureter (fig. 2, p. 21).

Radiographic examination after injection of uroselectan intravenously confirmed appearance of almost normal renal pelvis and greatly dilated ureter on left side. Right side not clearly visualized. The uroselectan was held up in the left ureter to such an extent as to be still clearly visible outlining the ureter, three hours after the injection.

Cystography.—Showed normal bladder with sodium bromide entering left, but not right, ureter. Second attempt at catheterization of ureters one week ago: turbid, blood-stained urine obtained from left renal pelvis; on culture this yielded *Staphylococcus albus* only. It was not found possible to pass a catheter up the right ureter.

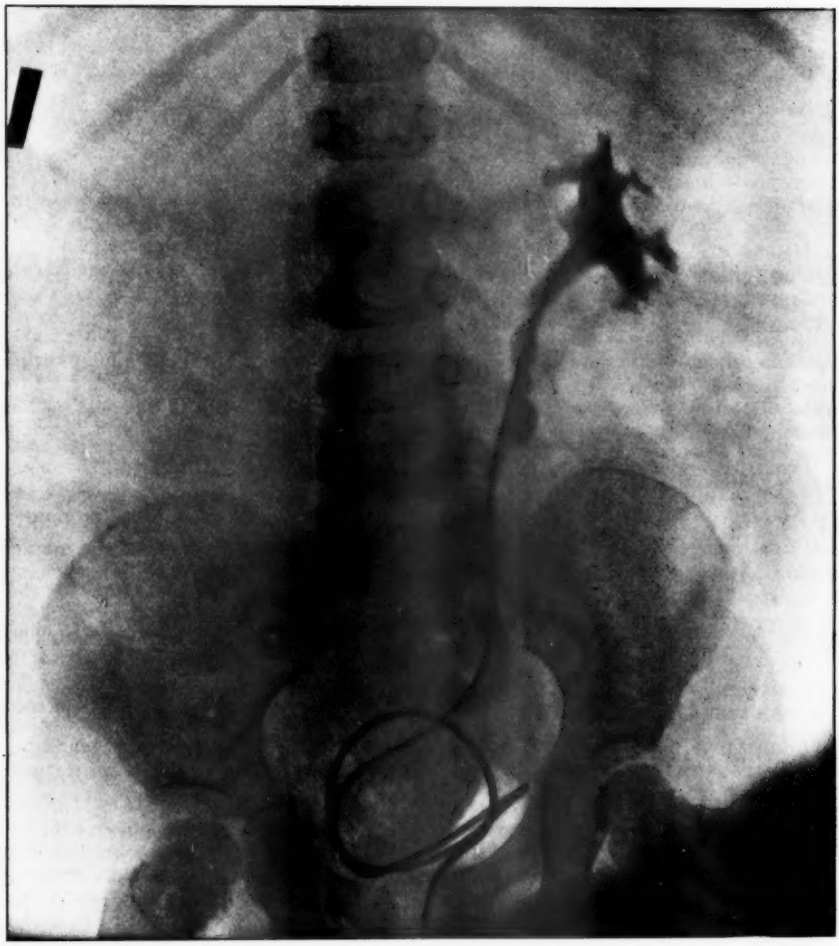


FIG. 1.—Right pyelogram, showing dilated ureter with ureteric catheter in situ.

(*Dr. Horsford's case of Congenital Dilation of Ureter*).

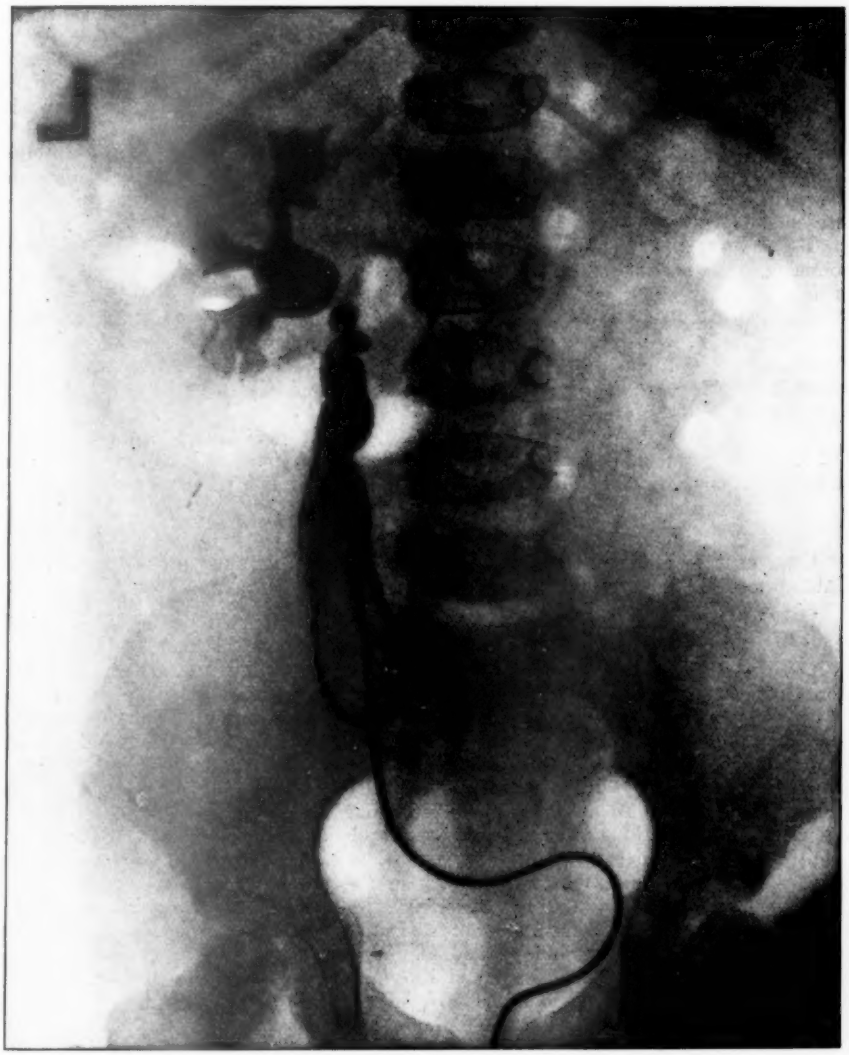


FIG. 2.—Left pyelogram, showing ureteric catheter coiled up in ureter.

Specimen of Complete Genito-Urinary Tract from a Case of Congenital Absence of the Abdominal Muscles.—JOHN GIBBENS, M.R.C.P.

Male infant, born July 16, 1930. One of binovulvar twins, born at thirty-sixth week. Mother had pre-eclampsia. Vertex presentation. Birth weight, 4 lb. 10 oz. Congenital absence of abdominal muscles noticed within an hour of birth : completely atonic abdomen, but slight feeling of resistance in the midline, so recti muscles probably present. Both kidneys easily palpable but not enlarged ; bladder easily felt as a large firm prominent tumour which contracted occasionally and extended up to the umbilicus. Liver easily palpable, but not enlarged ; spleen not felt. No spina bifida. Intestinal coils easily visible and palpable, especially when peristalsis occurred. At one period a mass was palpable in the right hypochondrium—probably intestine. Cord normal.

He was watched for two months and then had a severe attack of diarrhœa and vomiting, from which he died. At no time was there any albumin or pus in the urine. Normal gain in weight.

Post-mortem.—No trace of recti, or of internal or external oblique muscles seen macroscopically. Quadratus lumborum and erector spinæ normal. No abnormalities found apart from the genito-urinary tract, which shows: (1) great hypertrophy and dilatation of bladder ; (2) marked hydro-ureter ; (3) undescended testicles. There is no obstruction in the urethra.

The only explanation which I know of the condition is given in an article by Dr. Poynton, namely, that at one stage of intra-uterine life the ureters are much larger than they are in the child, and that this condition is a persistence of that.

Congenital Deformities with Stippled Epiphyses and Congenital Cataract.—R. C. LIGHTWOOD, M.D. (for HUGH THURSFIELD, M.D.).

R. W., male, aged 11 months, only child of healthy parents, has not been growing properly from the time of his birth. Present length, 23 in.

Clinical examination.—Head : occiput and vertex rounded ; forehead square ; frontal bossing ; maximum circumference of head 19 in., anterior fontanelle 2 in. by 1½ in. Palate high and arched. One lower incisor just erupted. Skin of face and head dry and scaly. Double congenital cataract. Thorax : backward displacement of sternum and costal cartilages, producing beading of the scorbutic type. Limbs : arms and legs short, as in achondroplasia ; this is due to the shortening of the humeri and femora. Measurements : upper arm 3½ in., forearm 3¼ in., thigh 4½ in., leg 4¼ in. Fingers long and tapering ; wrist held flexed and thumb drawn in. Limitation of movement at hip-joints, extension, external rotation, and abduction being difficult. Feet normal.

Radiographic examination reveals striking abnormalities of which the main features are as follows : Humeri mushroomed at both ends. Epiphyses stippled and shafts short. Forearm and hands normal. Femora show less stippling than do humeri. Femoral necks abnormally ossified and hips appear to be congenitally dislocated. Skiagrams taken when the child was 7 months old (figs. 1, 2, 3), showed much stippling of lower femoral epiphyses ; now, upper tibial epiphyses are markedly stippled. Otherwise bones of legs and feet are normal. Ossification in necks of ribs and in vertebræ is abnormal and there is stippling of epiphyses of pelvis.

Comment.—H. A. T. Fairbank has described two similar cases, one of these was unilateral, the other bilateral.[1] At a meeting of the Section of Orthopædics,

[1] H. A. T. Fairbank, *Brit. Journ. Surg.*, 1927, xv, 57.

FIG. 1.—Congenital bone deformities with stippled epiphyses. The legs at age of 7 months.

FIG. 2.—Right arm at age of 7 months.

FIG. 3.—Left arm at age of 7 months.

(*Dr. Lightwood's case of Congenital Deformities with Stippled Epiphyses*).

St.J. D. Buxton recently showed a dwarf with stippled epiphyses.[1] The pathology of the condition has not been worked out, nor has a name yet been given to it.

The parents of this child were first cousins.

POSTSCRIPT.—The child died a few days later, suddenly, and at autopsy was found to be suffering from an acute miliary tuberculosis.

Congenital Opacity of both Corneæ with Slight Buphthalmos.—F. PARKES WEBER, M.D.

This case is shown as an example of developmental abnormality. The child (female, aged seven weeks) appears to be normal, except in regard to the eyes. The mother, aged 23 years, whose Wassermann reaction is negative, has had only one other child (living and healthy); no miscarriages. Both eyes are slightly enlarged and their intra-ocular pressure is increased; the outer border of the cornea is not sharply defined. Both corneæ are bluish-white, and in the central portion of each is a disc-like

[1] St.J. D. Buxton, *Proceedings*, 1930, xxiii, 1329 (Sect. Orthopædics, 53).

area of greater opacity. In the middle of this disc in the left eye is a staphylomatous protrusion. The child can distinguish light from darkness. The mother was apparently in perfect health during pregnancy and there is no suspicion of any "avitaminosis A." The father is a milkman and there has always been plenty of milk and no lack of food; margarine has never been used by the mother instead of butter. There has never been any discharge or other sign of active inflammation in the child's eyes, at or since birth. According to W. Gilbert (Pfaundler and Schlossmann's *Handbuch der Kinderheilkunde*, third edition, 1927, p. 67) the condition seems to be due to a defective development of Descemet's membrane, with apparently, in a case like the present, involvement of ciliary bodies. For microscopical examination bearing on the subject see E. Treacher Collins, *Trans. Ophthal. Soc. United Kingdom*, 1909, xxix, p. 169, and (with A. C. Hudson), 1913, xxxiii, p. 158. Dr. Iven, for whose help I am indebted, tells me that on the Continent he saw a child with similar corneal opacity, which, however, was not congenital, but had developed within the first few weeks of extra-uterine life. In that case it was suspected that the morbid process had really commenced during intra-uterine life—perhaps as a result of avitaminosis—but had not become obvious till soon after birth.

Section of Neoplasm shown at October meeting as ? Endothelioma of Foot.—ERIC I. LLOYD, F.R.C.S.

The large mass between the toes was encapsuled, but shelled out fairly easily. I think it will be agreed that it is a fibro-sarcoma and not an endothelioma.

[*January* 23, 1931.]

Ataxia of Cerebellar Type following Diphtheria.—C. WORSTER-DROUGHT, M.D., and T. R. HILL, M.D.

D. L. A., female, aged 15 years. The patient exhibits signs of generalized incoördination which dates from an attack of diphtheria in 1919, at the age of 4 years. There is also some mental retardation which is made to appear worse than it actually is by severe dysarthria.

History.—Occasional epileptiform attacks from age of 18 months onward; (?) rheumatic fever at 10 months; (?) tuberculosis left knee at 20 months; scarlet fever at 3 years.

December 2, 1919: Onset of attack of faucial diphtheria, small patches of membrane being present on both tonsils. A week later several attacks a day of *grand mal* developed and the patient became semi-comatose. This stupor gradually passed into drowsiness and disorientation which lasted for six months.

After fourteen days of illness the fits ceased, but the plantar reflexes were stated to be extensor and the tendon reflexes exaggerated. Pupils and discs normal. Much generalized muscular weakness and emaciation developed. Cerebrospinal fluid normal. After two months, jerky movements of limbs and grimacing were observed. Legs held in flexion at hips. No tendon reflexes elicited. After seven months, drowsiness and disorientation diminished. Patient took interest in general things, made noises and laughed, but did not speak. Power in arms fair. Could not sit up. Legs weak and often held in flexion. After eight months, discharged from hospital with generalized jerky and spasmodic movements, impaired mentality, sluggish tendon-reflexes, and a tendency to hold legs flexed at hips.

Present condition.—Mental state: Inactive, sits still all day; talks very little; obeys commands; memory normal.

Nervous system: Pupillary reactions normal. Vision, fields and discs normal; concomitant strabismus; bilateral slow nystagmus and restless movements of eyeballs. Marked dysarthria. Occasional grimacing, tremor of head and slight

narrowing of left palpebral fissure. Sensation normal. Motor system: Slight hypertonia in arms and legs. Intention tremor, ataxia, dysmetria, and asynergia marked in all limbs. Dysdiadokokinesia marked. Power fair, arm-jerks brisk and equal. Reflexes; Abdominals sluggish and equal; plantars flexor; knee-jerks exaggerated, right greater than left; ankle-jerks sluggish and equal; no clonus. Occasional incontinence of urine. Gait: ataxic and reeling. Cannot walk without assistance. Stands and walks on a wide base. Other systems normal. Cerebrospinal fluid normal, with negative Wassermann reaction. Blood Wassermann reaction negative.

We are indebted to Dr. Borthwick, Medical Superintendent, Northern Hospital, Winchmore Hill, for permission to record this case.

COMMENT.—The special interest of the case is that it presents a problem in ætiology. The dysarthria, ataxia and motor impairment date so definitely from the attack of diphtheria that it is difficult to exclude some causal relationship. One suggestion is that, taking into consideration the patient's previous history, which is apparently normal apart from occasional epileptiform attacks, she is possibly the subject of one or more congenital aneurysms on cerebral or cerebellar arteries (which might account for the pre-existing epilepsy), and that during the course of the diphtheria one such aneurysm may have ruptured, causing an extensive lesion of the cerebellum and deeper parts of the brain. Against this view, however, is the fact that such hæmorrhages are usually subarachnoid, whereas the history and present condition do not favour a diagnosis of spontaneous subarachnoid hæmorrhage. A diffuse encephalitis, either diphtheritic or as the result of a coincident infection, is also a possibility. Apart from peripheral neuritis, however, the most frequent complication affecting the nervous system in diphtheria is cerebral embolism or thrombosis. An extensive thrombosis mainly of cerebellar arteries, with consequent softening, appears the most probable explanation in this case. A similar problem was presented by a case of bilateral hemiplegia complicating diphtheria which we showed earlier in the session.[1]

Discussion.—Dr. J. D. ROLLESTON said that, in his opinion, this was a unique case. In the discussion on the case which Dr. Worster-Drought showed at the last meeting (one of double hemiplegia following diphtheria) the question of encephalitis was raised and he (Dr. Rolleston) had remarked that encephalitis had been suggested as a cause of hemiplegia in diphtheria, as could be seen from Dynkin's paper,[2] 1913 and Querido's[3] case in 1928. But as none of these cases had come to autopsy it could not be verified.

Dr. WORSTER-DROUGHT in reply said there was no doubt that the present condition began during the course of the diphtheria; there was no previous history of incoördination, dysarthria or any nervous lesion beyond the occurrence of the occasional epileptiform attacks. With regard to heredito-familial ataxia the onset of the present disorder was more sudden than gradual and there is no family history of a similar condition; also the knee and ankle jerks are present and there is no hypotonia; the limbs, in fact, are rather hypertonic and such hypertonia appears now more extrapyramidal than pyramidal. If the condition had not dated so definitely from the diphtheria and had shown occasional remissions, a diagnosis of disseminated sclerosis beginning at an unusually early age might also have been considered. The Lange reaction in the cerebrospinal fluid was negative and did not suggest this condition.

Dwarfism with Mental Defect.—K. H. TALLERMAN, M.D.

G. H., female, aged 3 years and 9 months, was brought to hospital because of her small stature, and inability to speak properly.

Family history.—Nothing significant. One other child, healthy and normal.

Past history.—Child was said to be a full-term infant; instrumental delivery;

[1] *Proc. Roy. Soc. Med.*, 1931, xxiv, 350 (Sect. Dis. in Child., 12.)
[2] *Jahrb. f. Kinderheilk.*, 1913, lxxviii, Erg. Heft, 281.
[3] *Nederl. Tijdschr. v. Geneesk.*, 1928, i, 181. (Also in *Medical Annual*, 1929, xlvii, 131.)

birth weight 4½ lb. She was unable to suckle properly as an infant, and so was fed on a cow's milk dilution by means of a spoon. She is now taking an ordinary diet. Teething began at about the age of 1 year. Patient did not walk until she was 2 years old, and does not now talk normally; is apparently clean in habits. Has always been in good health.

On examination.—The child is extremely small, being only 2 ft. 7½ in. in height. though her limbs are properly proportioned; she weighs 20½ lb. The circumference of the head is 18¾ in. The epicanthic folds are abnormally prominent, the left more marked than right. Teeth all carious. Hypertrophy of tonsils. Apart from the above there are no abnormal physical signs except definite strabismus. Urine normal; blood-urea 35 mgm. per 100 c.c. of blood. A skiagram of skull shows sella turcica to be normal. Wassermann reaction negative. No abnormality noted in stools; bowels open regularly. The child, who seems healthy, is quite content and placid, but appears to be definitely mentally defective.

Hyperthyroidism.—I. W. GALLANT, M.B. (for Dr. DONALD PATERSON).

G. W., female, aged 10 years and 1 month. Born in Enfield and has always lived there. Previous illnesses, measles, chicken-pox, whooping-cough.

Onset.—When 8 years old, two attacks of "vacancy" at school: fell and became unconscious; vomited, then fell asleep; duration 15 minutes; general nervousness.

FIG. 1.—G. W., at age of 8 years.

Condition in September, 1929.—Bilateral exophthalmos; von Graefe, Joffroy, Moebius and Stellwag signs present: fine tremor, headaches, pulse-rate 92, no clinical enlargement of heart; thyroid moderately enlarged; nervous irritability; weight 57 lb.; no X-ray evidence of thymic enlargement; urine normal, emotional control good, no digestive disturbance.

Progress.—Stationary, with slight fluctuation : sleep poor. Has been to convalescent homes for eight weeks on two occasions with obvious improvement. Returned from Brentwood in October, 1930; weight 70 lb.; less nervous, slight exophthalmos with Joffroy's sign ; tremor slight ; no headaches ; thyroid enlargement almost disappeared, pulse-rate 90, weight 70 lb.

FIG. 2.—G. W., aged 4 months.

Dr. DONALD PATERSON said that the interest of this case lay in the long duration of the symptoms, the condition having lasted for eight years, and been active for two years. The patient had been having 5 minims of tincture of iodine three times daily for more than a year, and smaller doses in the previous year. There was now a gradual improvement, but that might be simply because she was "growing out of it" rather than being cured by the iodine. He (Dr. Paterson) thought this must be classed as a case of toxic hyperthyroidism. The thyroid gland had never been really large, that was to say it was not goitrous.

Polycystic Kidneys.—D. J. TURNBULL, L.R.C.P., M.R.C.S. (for Dr. A. G. MAITLAND-JONES).

F. L., a boy aged 10 years. An only child.

There is no family history of any significance. From birth until age of 3 years is said to have suffered from fits ; these were only of a few seconds' duration but he used to fall down and the limbs became stiff. At age of 3, these attacks ceased completely. From that age onwards suffered from periodical vomiting attacks (three to twelve weeks) which occurred without nausea, generally speaking, after which he felt quite well. From age of 6 years, slight abdominal pain has sometimes accompanied these vomiting attacks which for the past two years has been getting worse, although he has never been confined to bed during one of them. Apart from above and an attack of pneumonia at age of 5 years, has always been well. Only occasionally suffers from headaches, which are not severe. No urinary symptoms. He is intelligent and has always been fat.

On examination [December 10].—The boy, who is very obese, appears healthy. *Abdomen*: two large tumours felt, that on right side much larger than that on left. Right-sided tumour can be palpated bimanually; it can be felt emerging from under costal margin in line of right sternal edge and continues downwards one finger's breadth below the umbilicus and back into the loin. The tumour on the left admits a hand between it and the loin, and extends down four fingers' breadth below the costal margin in the anterior axillary line; some tenderness over both tumours. No ascites present. Genitalia are definitely small. Optic discs show slight degree of chronic papillœdema and atrophy, otherwise no abnormality to be found; visual fields normal. Deep reflexes are normal. Skiagram of skull shows no abnormality of sella turcica. Blood-count normal. Urine contains a trace of albumin and occasional red cells and leucocytes, but the renal efficiency tests are normal (blood-urea 0·24 mgm. per 100 c.c. of blood). Skiagram shows a large shadow in both loins, the right appearing enormous in size. Wassermann reaction negative. Blood-sugar curve (12.1.1931) showed: fasting level 0·07%; half-hour after 50 gm. glucose 0·177%; 1½ hours after the sugar 0·1%. No specimen of urine taken during the progress of the curve gave a reduction with Fehling's solution.

During the stay in hospital the boy has seemed perfectly fit although he has vomited on three occasions. Fluid intake and output show no definite abnormality.

Re-examination of the fundi on January 15 showed bilateral papillœdema, +4·0 dioptres right, +2·0 dioptres left. Blood-pressure 150/90.

The calices of the right kidney are splayed out more than is normally the case, and this fact supports a diagnosis of polycystic kidneys. The left kidney secretes far more of the uroselectan than does the right.

Discussion.—Dr. H. L. TIDY said that this case was more probably one of bilateral tumours of the cortex of the suprarenals. This diagnosis would agree with the sharpness of the intelligence and the obesity.

Dr. W. M. FELDMAN said that, in view of the fact that the renal efficiency seemed to be normal and the blood-urea within normal limits, this was probably not a case of polycystic kidneys. The blood-pressure in this child of 10 years was 150/90; whereas with bilateral suprarenal tumours one might expect the blood-pressure to be below rather than above normal. There was the further fact in the case that there was definite bilateral papillœdema, which favoured this being some renal disease, rather than suprarenal.

Dr. F. PARKES WEBER said that the case seemed to be a puzzle, because if it was one of bilateral congenital polycystic kidneys, it would be unusual to find symptoms due to renal deficiency coming on so early. He did not think, however, the diagnosis of polycystic kidneys could be excluded; the boy's fatness might be an independent condition.[1]

Dr. MAITLAND-JONES (in reply) said that he was responsible for the original diagnosis and nothing that had been said in the discussion had induced him to change his opinion.

Thrombocytopenic Purpura. Post Splenectomy.—B. F. M. BOND, L.R.C.P., M.R.C.S. (for Dr. DONALD PATERSON).

Patient, a girl aged 6 years, admitted to hospital September 15, 1930, with two weeks' history of three severe attacks of epistaxis. No previous history of abnormal bleeding, spontaneous bruising, or painful joints.

Condition on admission.—Few scattered petechiæ on back, abdomen and limbs. Spleen not palpable. Heart: Apex beat in fourth space ¾ in. outside nipple line. Tic-tac rhythm. Basal systolic murmur.

Blood-count.—R.B.C.s, 2,143,000; Hb., 45%; C.I., 1; W.B.C.s, 7,200; polys., 62%; monos., 6%; lymphos., 32%; platelets, 125,000. Patient bled profusely from ear when pricked for blood-count.

1 As a more likely diagnosis Dr. Weber suggests diffuse lymphoblastic ("lymphosarcomatous") infiltration of both kidneys, or bilateral embryonal "mixed tumour."

Continued epistaxis (in spite of repeated plugging) and hæmatemesis necessitated blood-transfusion from mother (24.9.30).

Splenectomy performed by Mr. Tudor Edwards (26.9.30). The organ was adherent posteriorly and weighed 60 grm. Report by Dr. Braxton Hicks:—

"General increase in connective tissue, and splenic pulp appears as an open sponge, particularly at the periphery. The lymphocytes have for the most part disappeared, with the exception of the Malpighian corpuscles."

The patient was transfused before and after operation.

Subsequent course.—Epistaxis recurred 3.10.30, necessitating transfusion. Since then, there have been repeated, moderately severe attacks of epistaxis, and recurrent crops of petechiæ with excessive bruising. No epistaxis for past month.

Patient was given intensive daily treatment with mercury-vapour lamp, by Dr. H. Mansell, from 10.10.30 to 5.11.30, reaching exposure of 25 min. front and back at 14 in. On recurrence of epistaxis (25.11.30) three intramuscular injections of normal horse serum were given patient (7.12.30, 15.12.30, and 27.12.30). Severe but transitory pain occurred 48 hrs. after the second injection, and a very fine purpuric eruption after the last.

Platelet-count fell from 125,000 c.mm. (16.9.30) to 6,000 (21.10.30) with a subsequent rise to 45,000 (16.12.30). The coagulation time was normal throughout. The bleeding time has varied from 18 min. (15.10.30) to 7½ min. (27.10.30) with a subsequent increase to 23 min.

Our point in showing this case was to indicate that those who suggest removal of the spleen in states of thrombocytopenic purpura are sometimes over-optimistic. This was one of the acute cases. The child was very ill, and had to be transfused on several occasions, otherwise she would have died. Removal of the spleen made her, if anything, worse than she was before, and we despaired of saving her life. We continued with the transfusions, and gave massive doses of liver extract by the mouth, but without apparent influence. The disease gradually burned itself out, and improvement ensued, the platelets coming back to normal. There are now recurrent fine petechial hæmorrhages, but there is no oozing of blood from the mucous membrane of nose or gums. Last week a tooth came out; there was a little oozing for 12 hours, then it ceased.

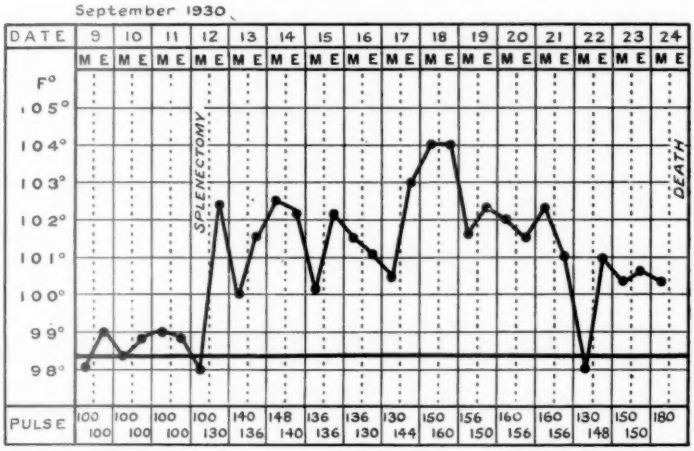
Discussion.—Dr. H. L. TIDY said that this case might still have a successful ending. Hæmorrhages might persist for some time after splenectomy and then cease. It had been correct to operate because operation gave the best chance of recovery in the circumstances.

Dr. WILFRID SHELDON said so much was heard about the good results of splenectomy that he would like to relate a case which proved a catastrophe. It was that of a boy, aged 6 years, whom he had observed for two years in his out-patient department. The boy always showed purpuric hæmorrhages in the skin, and occasionally passed blood per rectum. The tonsils had been removed, and other foci of sepsis had been sought in vain. In September, 1930, the blood-count was normal, except that the platelets only numbered 50,000 per c.mm. The coagulation time was 1 min. 50 secs., the bleeding time was 36 min., the capillary resistance was positive. Although the spleen could not be felt, the case was regarded as falling into line with those for which splenectomy had been advised. On September 12 the spleen was removed. The events which followed are given in chronological order.

12.9.30: Splenectomy, followed by blood transfusion of 235 c.c. 14.9.30: Acetonæmia, countered by giving glucose. 15.9.30: Slight icterus. 17.9.30: Signs of consolidation over left upper lobe of lung—child flushed, and of florid complexion. 18.9.30: Jaundice deeper. No evidence of obstructive type of jaundice. 20.9.30: Crepitations over left lung which seemed to be beginning to resolve. 21.9.30: Left lung clearing. Within twelve hours the colour has changed to one of intense anæmia. Blood transfusion of 235 c.c.

22.9.30: 8 a.m. Anæmia again intense. R.B.C.s, only 930,000 per c.mm. Liver enlarging, reaching to umbilicus. Blood transfusion of 300 c.c. Immediate improvement

noted. 4 p.m.: Anæmia again intense. R.B.C.s, 1,500,000 per c.mm. Liver now down to iliac crest. Dullness over base of left lung. The abdomen was re-opened to exclude the possibility of a secondary hæmorrhage, but no blood was found. There was, however, a very small *B. coli* abscess behind the left lobe of the liver, containing less than a thimbleful of pus. The abdomen was drained, and another transfusion of 200 c.c. was given. The dull area at the base of the left lung was explored with a needle, and 30 c.c. of yellow serous fluid was



Temperature chart.

withdrawn, which proved to be sterile. 23.9.30: Child weaker. R.B.C.s, 2,250,000 per c.mm.; the film showed the presence of a few normoblasts. 24.9.30: Jaundice persisting. Death. At post-mortem examination there was no secondary hæmorrhage. The liver was very big, and pale, and showed fatty degeneration. The left lung was partially collapsed, with some fibrinous exudate over the lower lobe. (The spleen removed at operation appeared to be perfectly normal).

Dr. FINDLAY said that if splenectomy had any virtue in diminishing the tendency to bleed, it should be performed at the earliest moment after the disease was recognized. If he believed the modern teaching on the subject then he would do exactly what Dr. Paterson did, i.e., operate early. Dr. Tidy said it would be necessary to wait two years before expressing an opinion on the wisdom or otherwise of operation, but it might be necessary to wait ten years. He (the speaker) had had a case in a child with severe purpura (platelets 40,000). Splenectomy was advised, but the parents would not permit it. The patient apparently recovered, but six years later she returned, having as severe an attack as the previous one. The spleen was removed, and the bleeding, which had ceased the night before operation, began again immediately afterwards, and the platelets steadily fell. Was the explanation that in acute cases the patients died, and that splenectomy did no harm in the chronic cases in which the patients would have lived in any event?

Coarctation of the Aorta.—WILFRID SHELDON, M.D.

Patient, a girl, aged 2 years and 2 months, was brought to the Hospital for Sick Children, Great Ormond Street, on account of poor appetite and failure to gain weight. No history of attacks of breathlessness or cyanosis. The mother was unaware that the heart was in any way abnormal.

Condition on examination.—The child is puny and under weight (weight 23 lb.). She is not cyanosed, nor are her fingers clubbed. Apart from the cardiovascular

system, no abnormal physical signs have been discovered. The heart is not enlarged, but there is a systolic bruit audible over the præcordial area, reaching its maximum intensity just under the left clavicle and conducted thence up along the vessels of the neck, along the subclavian vessels, and posteriorly down the line of the descending aorta to the lower thoracic vertebræ. The murmur is not accompanied by a thrill. Pulsation of the carotid arteries in the neck is obvious, and an unusual degree of arterial pulsation can be seen in the episternal notch, while the radial pulse can be easily felt. No pulsation can be felt in the abdominal aorta, or in the femoral, popliteal, or dorsalis pedis arteries. The blood-pressure in the right arm is 120 systolic, 90 diastolic. In the right leg the systolic pressure is ? 100; the diastolic pressure could not be determined. No evidence of a collateral circulation—such as pulsation of the posterior scapular, long thoracic, or epigastric arteries, can be made out. A skiagram of the chest confirms the normal size of the heart.

(This patient is under the care of Dr. Bernard Schlesinger, and I am indebted to him for permission to show her).

The fact that the heart is not enlarged and that there is no collateral circulation might be taken to signify that the constriction of the aorta is of only mild degree. But according to Dr. Abbott, who wrote an article on the subject in "Modern Medicine," neither the size of the heart nor collateral circulation affords any evidence of the degree of constriction of the aorta.

[Dr. FINDLAY: I suppose this is the earliest age at which this has been recognized clinically ?]

As far as I am aware, this is the youngest case on record of the "adult" type of aortic coarctation. The "infantile" type, in which there is a gradual narrowing of the aorta over a considerable length, is generally fatal shortly after birth.

Hereditary and Familial Oxycephaly.—WILFRID SHELDON, M.D.

Mrs. E. H. and her three children have been under observation in the Children's Department of King's College Hospital for several years. Mrs. H. is very definite about being able to trace back her facial appearance to her father, now dead, whom she closely resembled. Her three children, Ivy, Stanley, and James, bear a striking resemblance to each other and to their mother.

Mrs. H., aged 42 years, has eyes set far apart, the outer canthus being lower than the inner. Her forehead is unusually high, and from the occipital protuberance the skull rises in an even incline to the apex of the forehead. The X-ray appearance of the skull confirms the oxycephalic shape, and shows to a mild extent in the frontal bones the mottling so characteristic of this condition (fig. 1).

Ivy, aged 14 years, the first representative of the next generation, shows to a more marked extent the wide separation of the eyes. The skull has the same shape as her mother's and the X-ray picture again shows the mottling of the membrane bones (fig. 2).

Stanley, aged 11 years, shows the condition more advanced than the others. His eyes are wide apart, and there is lateral bulging of the temporal bones just above and in front of the ears. The forehead rises upwards and slightly forwards, so as to overhang the face to a slight extent. The mottling of the skull bones is very well shown (fig. 3).

James, aged 7 years, has less temporal bulging than his brother, but the overhanging of the forehead is more evident. The apex of his skull is not thrust quite so far forward as in the other members; mottling is seen in the frontal and parietal bones (fig. 4).

The mental development of the mother and her children has not been impaired by the skull deformity. No other children—no miscarriages.

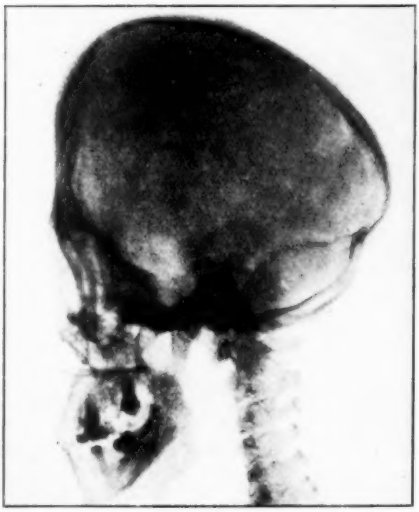


FIG. 1.—Mrs. H., aged 42 years.

FIG. 2.—I. H., aged 15 years.

FIG. 3.—S. H., aged 11 years.

FIG. 4.—J. H., aged 7 years.

Section of Urology.

[*January* 22, 1931.]

The Significance of the Radiological Renal Outline.

By S. Gilbert Scott, D.M.R.E.

Many of you may consider the limit of the radiological examination of the kidneys—if accessory methods of examination, such as pyelography ascending or descending, be excluded—to be the demonstration of a calculus. The field of usefulness is, however, very much larger than this.

As a matter of interest, I originally read a paper on "The Significance of the Radiological Renal Outline" at Cambridge in 1920 before the Radiological Section of one of the British Medical Association meetings. I afterwards realized that the subject had been brought up several years too soon, as there were then but few radiologists who possessed the technical skill necessary to demonstrate the renal outline—an essential requirement.

The technical side of radiology has made such rapid strides in the last few years that this difficulty no longer exists. In fact nowadays no radiological examination of the urinary tract can be considered complete or satisfactory unless the whole of the kidney is demonstrated. In many cases the shadow of the suprarenal gland is even discernible. The improvement in X-ray tubes, screens, and films, the Potter-Bucky diaphragm, and the production of electrical transformers capable of large output, making rapid exposures possible, have all contributed to this advance in technique.

It is, however, obvious to the more experienced radiologist that the general standard of diagnostic accuracy and skill has not reached the high pitch of excellence of technique. This is quite understandable, as it is now possible for anyone possessed of average intelligence to produce first-class radiographs after only half a day's instruction in the use of present-day apparatus. There is consequently a tendency for the radiologist once again to be looked upon, as in the early days of radiology, more as a glorified photographer than as a diagnostician. The skill of the radiologist appears often to be gauged by the number and size of the films he brings forth—both are expected to be as large as possible. His deductions, on the other hand, which should be considered the all-important part of the examination, are frequently ignored.

The primary object of the radiologist should be to extract every atom of accurate information from his examination and to pass the findings on to those concerned in a clear and concise form—his films being used simply to demonstrate and record the evidence on which he has based his diagnosis. It follows that he must have at his command the highest technical skill in addition to experience.

Radiological errors are of two types—those of affirmation and those of negation, the greater and commoner of these being those of affirmation, for here the discovery of a lesion which is non-existent frequently leads to the carrying out of an unnecessary operation.

The sin of affirmation is one of inexperience and unfamiliarity with the numerous radiographic pitfalls.

In this country, Dr. MacIntyre of Glasgow was the first to publish the fact that renal calculi could be detected radiographically. Since then, many a perfectly good kidney has been explored unnecessarily, on account of a shadow *appearing* radiographically to be a renal calculus. To-day any opacity can—and in fact

must—be proved to be either intra- or extra-renal in origin. I will later indicate a method by which it is possible to prove whether or no a shadow is of renal origin, and so reduce the possibility of mistakes.

I consider this particular examination, where the object is to show the shadow of a soft tissue organ—the kidney—against a background of almost equal density, namely, muscles of the back, to be one that demands precise technique, for the margin of error is small. Faulty preparation, any movement of the patient or tube, incorrect exposure or development of the film—and the renal outline will be looked for in vain.

From a host of minor details I will mention two which I consider essential: (1) Efficient clearance of the bowel of fæces, flatus and fluid. (2) Efficient abdominal compression by means of the "sugar-loaf" cushion which I have designed especially for this purpose.

It is a common error to think that full abdominal compression, even if efficiently applied, results in the complete immobilization of the kidney. Actually, compression applied over a kidney, normal in size and position, in no way restricts its respiratory excursion. Why, therefore, do I stress the importance of compression? The answer will be obvious if the effect of pressure on the abdomen is observed under the fluorescent screen. There will be noted a definite clearing of the field, with an increase of shadow values, probably explained by the emptying of blood-vessels and displacement of the intestines, or their contents, by the pressure.

Extra fine detail is obtainable if each kidney is radiographed separately, and this method should be used if the suprarenal gland is to be demonstrated.

Diagnosis.

To be able to state definitely that both kidneys can be seen radiographically to be normal in position, shape, and size, is often of value. The information that the patient has radiographically only one kidney at once suggests the possibility of this being a solitary organ, or that its fellow is in some abnormal position.

Or again, take a case in which the kidney on one side is obviously badly disorganized, possibly containing calculi and pus, and its surgical removal is probable—the presence and condition of the remaining kidney becomes one of vital importance, and should be ascertained in spite of other methods that may be used to find the functioning index.

To be in a position to appreciate any pathological alteration in shape or size of the kidney, it is necessary to be familiar with the various types of kidney, which, while differing from the average shape, are yet merely varieties of the normal and of no pathological significance.

I recognize three types: the globular, the elongated, and the lobular. The globular is a rounded type, nearly as broad as it is long—a type that may easily be misinterpreted as enlargement. As the name implies, the elongated is a long and narrow kidney. The lobular type has a wavy outline, a reversion to the early or developmental stage. It is occasionally met with in the early stages of hydronephrosis. Personally, I always expect other congenital abnormalities with this type of kidney—such as an abnormal blood-vessel, valvular folds in the ureter, etc., which are frequently found in conjunction with it, or even faulty development of the skeleton, as, for example, a partial spina bifida, a condition met with in relation to the fifth lumbar vertebra. Any two of these types may be present in the same patient, irrespective of the build or make-up of the individual.

The position of the kidneys is somewhat variable, and the respiratory excursion of the kidney also shows an individual variability. In some cases the alteration in position between inspiration and expiration is only an inch, while in others,

especially in those trained in singing, the excursion may reach three inches. Use is made of this respiratory excursion for the localization of opacities. Whilst a slightly restricted respiratory excursion is of no pathological significance, an entire absence of movement would indicate fixation by adhesions due to perinephritis. As already mentioned, the actual degree of movement is variable in different individuals, but the mechanism is the same. Thus it is seen that the downward displacement of the diaphragm by inspiration depresses the liver or spleen, as the case may be. This pressure is in turn conveyed to the upper pole of the kidney. While the kidney now travels down as a whole, the lower pole swings outwards; this is the effect of pressure being exercised on the upper pole in a downward and inward direction. There is also a rotatory movement of the organ, bringing the renal pelvis forward; this movement, however, is not so important.

Kidneys abnormal in size.—It is not always an easy matter to decide when a kidney has actually passed the normal limits, in respect to size.

In children, the kidneys always appear on the film large in proportion to the size of the child and may erroneously suggest enlargement. This is explained, I believe, by the fact that development of the kidney is normally in advance of the rest of the body.

Hypertrophy. Uniform enlargement—that is, when the kidney is enlarged but retains its shape—is met with in hypertrophy, when the opposite organ, for some reason, has ceased to function or is absent.

Syphilitic kidney.—The diagnostic feature is an increased density as well as of size of the whole organ.

Hydronephrosis.—In the early stages—no alteration in size or shape is detected. Continued "back pressure" will eventually result in a general enlargement, often accompanied by lobulation, that is, a reversion to its developmental shape.

Pyonephrosis.—The diagnostic sign of pyonephrosis is the detection of pus shadows in an enlarged kidney. The shadow cast by pus has a definite character and is quite distinct from that cast by calculi.

A local bulging of the renal outline may indicate either a local hydronephrosis—cyst—or new growth, but without accessory methods of examination these cannot be differentiated.

Atrophic kidney.—A small atrophic kidney is seldom met with. As previously mentioned, the elongated type of normal kidney may erroneously suggest a functionless organ. If the kidney shadow is small, the cause is either congenital or acquired, usually being the result of renal tuberculosis. The most practical use to which the demonstration of the renal silhouette can be put is in those cases in which nondescript ill-formed opacities are present.

Formerly, when the position of the organ could not be determined, it was only possible to guess whether a given shadow was of renal origin, the correctness of the guess being dependent on the experience of the radiologist. It is obvious that if there is no indication as to where the kidney lies, the relation of the opacity to it is problematical.

Visualizing the organ, however, now makes it possible to determine whether the opacity is outside or within its limits, but even then, if it is located over the renal shadow, there is nothing to indicate whether the opacity is in front, behind or actually in the kidney.

Shadows cast by calcareous glands, gallstones, opacities in the intestines, pills, even a pancreatic calculus or a wart on the skin of the back, etc., may mimic renal calculi to a remarkable degree.

It was to obviate this source of error that about ten years ago I devised a method by which it was possible to prove definitely whether any given opacity was related

to the kidney. This method has saved me from many an erroneous deduction. For the want of a better term, I have called it "renal localization." It is a means of determining whether an opacity, however insignificant, is extra- or intra-renal, and this without the employment of any special apparatus. It is based on the assumption that "any opacity seen radiographically within the limits of the kidney outline must be of renal origin, if its respiratory excursion is equal to that of the kidney in extent and direction."

It will be understood, therefore, that the essential requirements are the demonstration of the kidney and the production of two radiographs, one taken at full inspiration and the second at full expiration.

No special apparatus or changing box is necessary for this, as the position of the film in all renal work should be standardized. These two radiographs are now placed side by side in the viewing box. It is at once obvious that the kidney is at its lowest level on the inspiratory radiograph.

Let us again study the respiratory excursion of the kidney, and at the same time watch the movement of an opacity in relation to it.

If we assume, in the first instance, that the shadow is not of renal origin, it will be noted, on comparing the two radiographs, that it has either "wandered" right off the kidney shadow, or, at any rate, has not kept its relative position.

In the second example, assuming the opacity to be of renal origin, it will be noted that it conforms to all and every movement of the kidney and always retains the same relation to it. In other words, its position in the kidney remains unaltered, whatever may be the movements of the kidney itself.

This method has proved its practical utility time after time, more especially in the early diagnosis of renal tuberculosis, when the only radiographic evidence will be a minute ill-defined shadow, which is often passed over as of no diagnostic significance. If, however, this can be located without any doubt, in the kidney itself, it at once becomes of importance and is, in fact, the key to the diagnosis.

It is often stated that the radiological examination cannot reveal renal tuberculosis in its early stage; the reason is that though the evidence is frequently in the radiograph, it remains unrecognized.

Another type of case in which the method is of value is that in which gallstones are present. It is not always safe to rely for diagnosis on the shape or density of the gallstones, as renal calculi occasionally give shadows indistinguishable from them. The radiograph, taken laterally, as advocated by some workers to assist the differential diagnosis, will be found of little practical value.

Several substances, such as potassium iodide, given orally, have been tried, with the object of increasing the density of the renal cortex, and, if possible, to outline the renal pelvis. While this is certainly accomplished by the intravenous injection of uroselectan or abridol, such a method cannot be used as a routine in every case. It would be a great advance in renography if some such non-toxic substance could be given orally to accomplish this.

Let me, in conclusion, make it quite clear that guesswork diagnosis in radiology, especially in determining the nature of opacities in the renal area, must be eliminated, and replaced by the more scientific and accurate methods now available.

Discussion.—Mr. JOHN EVERIDGE said that Dr. Scott had brought out important points. Many urologists were accustomed to localizing stones, and interpreting many of the pathological signs in the kidney by pyelography, and Dr. Scott now reminded them that finding by X-rays the outline of the kidney, in itself, demonstrated many of the pathological lesions. As to localization of stones by the method just described, one felt that in some cases the kidney was fixed, owing to perinephritis; in these cases the method would not be so satisfying and complete as by pyelography.

He made it a routine, in cases of "? stone," invariably to localize by pyelography, i.e., before attempting to remove a stone. Intravenous pyelography was now being used a good deal by urologists, and it was found to be very valuable.

Mr. FRANK JEANS said he agreed that the radiographer should not be regarded as a mere photographer. He thought that the surgeon who went against the opinion of the radiographer as to the presence or absence of stone, was asking for trouble. Years ago Mr. Thurstan Holland reached an accuracy of interpretation with 1 error in 200; it was probably now about 1 in 500. Even when the interpretation proved erroneous it was difficult to know whether the fault was the radiologist's or the surgeon's; sometimes it was the surgeon's.

Dr. E. J. H. ROTH said that one was not justified in assuming that, because the shadow of a body moved with the kidney, that body was necessarily in the kidney substance. There were a number of shadows which moved during the cycle of the kidney excursions, such as a calcified gland adherent to the kidney, or a perinephritic abscess, whilst, on the other hand, a floating calculus lying in the renal pelvis might be stationary in relationship to space as the kidney moved downwards. He had seen a number of errors arise from this apparently confirmatory procedure. The taking of a lateral radiogram, possibly with pyelography and stereoscopic radiography, was the most important method of localization of a doubtful shadow in the renal area.

The preparation of a patient for radiological examination of the urinary tract always presented some difficulty, and that difficulty was perhaps accentuated if morphine or some other drug had been administered. Castor oil was a good cathartic, but was apt to leave a quantity of gas in the colon. The partial retention of an enema was a more frequent occurrence than perhaps the radiologist realized. He (the speaker) thought that the best method of preparation was to give the patient a vegetable laxative on two successive evenings previous to the X-ray examination, and perhaps also to cut down the carbohydrate intake.

He did not think a radiologist should say that a kidney was normal in shape, size and position; the size and shape of a kidney could be only assessed if the radiograms had been taken at a distance of five feet, so that all distortion was eliminated, as in modern chest work. In the kidney region that was a difficult technical matter.

In the location of the kidney, compression was apt to be a matter of difficulty; unless patients were examined while in the erect posture, he did not think opinions as to the position of the kidney could be of very great value. He had found it easier to obtain a good renal outline in stout patients than it was in thin patients, and he thought the reason was that the stout person had more perinephric fat, which acted as a contrast medium to the kidney.

Radiography, was progressive, and that made one think of the possibility of the patient coming first to the radiologist for a diagnosis and then being sent by him to the urologist for treatment. The radiologist, however, was dealing with shadows, and in the case of doubtful shadows he could only give his opinion on appearances. He could not furnish a diagnosis; only by acting as a link in the clinical chain could the radiologist contribute to the best interests of the patient.

Mr. E. W. RICHES said that he would like to hear more about the preparation of the patient before the examination. Members had heard some of the methods usually tried, but still it was found that many radiograms were spoiled by the presence of gas in the bowel. It was usual to get better radiographs from out-patients than from in-patients, as the former were ambulant and active and there was less tendency for gas and fluids to accumulate and stagnate. In both classes of patient some improvement, from the point of view of the radiograph, could be brought about by giving charcoal on the night before.

Diagnosis by the method of noting the relative mobility of the kidney depended on seeing the kidney outline, therefore the due preparation of the patient became increasingly important. One did not always see the kidney outline as well as it was shown in Dr. Scott's series, and he would like to know what method of preparation Dr. Scott had employed in obtaining his renal skiagrams.

The effect of guess-work, even on the part of the radiologist, was seen sometimes. Not long ago he (Mr. Riches) had had such a case, which terminated fortunately. A patient had had right-sided renal colic, and on cystoscopy, blood was seen coming from the right side. The skiagram showed a shadow apparently in the upper pole of the kidney, which moved with the kidney and was reported to be a renal calculus. He explored the kidney, but could not find any calculus. There was, however, a small depression on the surface of the kidney, yellowish in colour, and hence he thought he was dealing with a tuberculous kidney, and accordingly took it out. On cutting it open, he found a very early hypernephroma. During the patient's convalescence another skiagram was taken, and the shadow was still there; he did not know what it represented.

Mr. CYRIL A. R. NITCH said that he was glad to hear Dr. Scott emphasize the importance of remembering that moles sometimes cast shadows; he had himself seen three cases in which a pigmented mole on the back projected a shadow in the renal area in patients who were being examined for suspected stone.

With regard to the localization of stone in the kidney, and the determination whether a shadow in the renal area was that of a stone in the kidney, his opinion was that nothing up to the present equalled a stereoscopic radiogram after the passage of an opaque catheter. One seldom saw shadows behind the kidney, and he did not know of any calculus material which could form in that site. Most of the shadows seen were in front of the kidney, and a stereoscopic radiogram would settle its position accurately. A pyelogram did not give the same information, because if the stone was small and was lying more or less loose in the pelvis, the opaque medium would immediately cover it and it might not be seen at all. The shadow lying in front of the kidney, if not a very dense one, would also disappear in a pyelogram. Therefore he relied on an opaque bougie and a stereoscopic radiogram.

Mr. CLIFFORD MORSON said that with the advance of radiology and pyelography there was a danger of forgetting that there was another picture besides the radiological, namely, the clinical. It was essential for urologists to bear in mind that, in the long run, accurate diagnosis was dependent upon clinical skill.

Mr. H. P. WINSBURY WHITE said that in the majority of cases of hydronephrosis, if the kidney outline was shown on the negative, it appeared as an enlarged tumour, and probably as a lobulated one, but he had in mind two cases in which not only was the kidney not enlarged, but it was even a little smaller than the normal size and was not lobulated. He was sure it would not be possible to diagnose those cases as being in any way pathological by means of a plain radiogram. Both were in women who gave a long history of right-sided pain—one for 12 years, the other for 14 years—and he made his diagnosis by pyelogram. In each instance, on removing the kidney, he found that the ureter had become obstructed by a blood-vessel, and this, added to the original cause, resulted in a considerable degree of atrophy, without thinning the renal substance in the usual way. Those two cases had been very instructive, and helped him to remember that renal enlargement in a hydronephrosis was not always to be expected.

Mr. JOCELYN SWAN said he admitted that tuberculosis of the kidney might occasionally be diagnosed from the appearance of small and indefinite shadows in a skiagram but he could not conceive of these being early cases of the disease, or cases which would not already have given rise to other clinical symptoms and attracted the attention of the surgeon to the disease before a small doubtful shadow appeared on the skiagram. Necessarily tuberculous disease of the kidney must be of some standing to give rise to areas of opacity on a film. This fact served also to amplify Mr. Clifford Morson's remark that the urologist's diagnosis should be arrived at much more by his clinical acumen than from such a link in the chain as the radiological examination, which should really only serve as a confirmatory procedure. Like Mr. Cyril Nitch, he (Mr. Swan) had found the greatest value from stereoscopic X-rays in these cases, and he would like to make a plea for a greater and closer co-operation between the surgeon and the radiologist.

There was another point worthy of discussion; Dr. Gilbert Scott maintained that any shadow which moved equally with the kidney during inspiration and expiration must necessarily be of renal origin, and this he (the speaker) denied. He could recall several cases in which a definite shadow in the renal area moved up and down equally with the kidney in its respiratory excursions; one of these was reported upon by the late Dr. Knox as probably a hypernephroma. Dr. Knox's view was perhaps justified because the patient gave a history of having had one attack of hæmaturia, and on routine examination he (Mr. Swan) had obtained a perfectly normal pyelogram. In this case the tumour was found to be a carcinoma of the splenic flexure of the colon which was adherent to the kidney. In another case an ill-defined shadow which moved equally with the kidney, proved to be a mass of softening, caseous, tuberculous glands. Therefore one could not place absolute reliance on the rule laid down by Dr. Scott with regard to a shadow synchronizing with the movements of the kidney. Such cases might be exceptional, but if the diagnosis had rested upon radiological findings, useless operations might have been carried out, whereas further urological examination would have shown the true nature of the lesion.

The PRESIDENT said that one of the most important points was that raised by Dr. Roth, concerning stereoscopic X-ray pictures. These were important not only in the case of the kidney, but also, and probably even more so, in connection with the elucidation of some pelvic shadows. In nine out of ten cases when there was a doubtful shadow in the pelvis in the line of the ureter, one could settle the question with a stereoscopic plate without employing a ureteric catheter at all, simply by noting the plane in which the shadow lay.

Another point raised by Dr. Roth was that of lateral skiagrams in doubtful kidney cases. Lateral skiagrams were most valuable, as they might show at once if the body casting the shadow was outside the line of the kidney, in which case no further investigation would be needed.

There was also the question of small shadows being seen in cases of early tuberculosis of the kidney. He did not know how these kidneys showing such slight shadows came to be radiographed at all, because the diagnosis of early tuberculosis of the kidney was not made from kidney symptoms: it was made by the cystoscope, and confirmed bacteriologically.

The importance of the renal outline during inspiration and expiration was a matter on which urologists had been insisting for a number of years. He believed it was first pointed out by Hurry Fenwick and Coldwell when the International Urological Association met in London in 1911.

The question of the radiologist as a photographer had been raised. He, the President, was not certain how far one wanted to take the opinion of the radiologist entirely. Personally, he always saw the radiographic plates when they were ready, and discussed them with the radiologist. The urologist had been trained in reading and interpreting skiagrams of the kidney and the urinary tract, and probably his experience was as large as that of the radiologist. One did not, however, wish to eliminate the radiologist, but rather to work in coöperation with him. The same could be said with regard to the pathologist. One wanted the facts, not these people's interpretations of the facts, for they were often wrong, as they had not the clinical aspect and records to help them, whereas the urologist had all these fixed in his mind.

Dr. GILBERT SCOTT, in reply, said that in cases in which the kidney was fixed, renal localization was still of value, as shadows outside the kidney would move off the fixed kidney and those within the kidney would remain stationary. He did not suggest that this method of renal localization should replace pyelography, either ascending or descending, but by practical experience he had found it an extremely useful everyday method, and of the greatest diagnostic value in the detection of early renal tuberculosis.

He had found stereoscopic methods of little value except in the examination of the ureters with an opague bougie in situ.

He did not wish to imply that this localization method was infallible, as the final diagnosis could often only be made after some accessory method of examination had been employed.

He agreed with the President that coöperation between the radiologist and urologist was of great importance. Surgeons should make a point of notifying radiologists when an error had been made, as one learned by mistakes if these were traced to their origin.

Section of Neurology.

[*January* 8, 1931.]

Chronic Sub-dural Hæmatoma.

By J. P. Martin, M.D., F.R.C.P.

Sub-dural hæmatoma may be defined as a collection of blood between the dura and arachnoid which has become encysted. By the kindness of Dr. Greenfield I am able to show you a specimen which he removed without rupturing the hæmatoma or detaching it from the meninges (fig. 1).

The patient in this case was a man aged 58. He felt well until five weeks before his death when he woke up one night with a sudden attack of vomiting. This continued for several days, amd was associated with intermittent severe frontal headache. From that time onward he gradually deteriorated mentally and physically

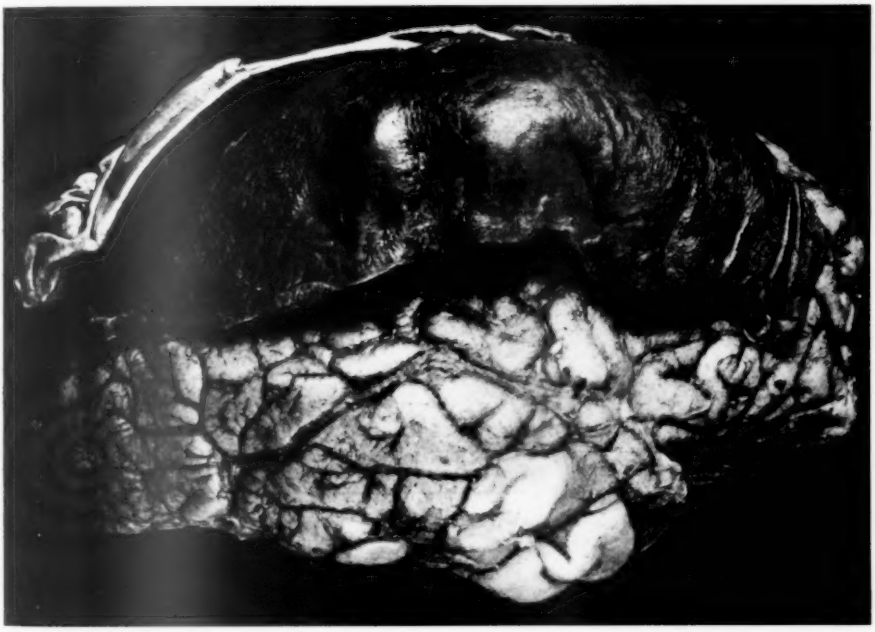


Fig. 1.—Subdural hæmatoma lying over the right cerebral hemisphere. Its contents were fluid when the specimen was obtained. The dura has been reflected, showing the underlying membranous envelope of the hæmatoma.

with symptoms to which I shall refer later. About a year earlier he had fallen when getting off a bus; he did not strike his head or sustain any evident injury and was at work as usual the next day.

Sub-dural hæmatoma was hardly known among the sane, except as a surprise finding at post-mortem examination or at operation, until a few years ago. Gowers called it a "pathological curiosity enigma." I say "among the sane" because it was well known as one stage or variety of the sub-dural hæmorrhage which is said to be frequently found post mortem in asylum patients and usually goes by the name which Virchow gave it—"Pachymeningitis hæmorrhagica interna." The clinical

recognition of chronic sub-dural hæmatoma and the knowledge of its curability we owe largely to Trotter, who in 1914 described four cases in which he had operated, in the last two of which he had made the diagnosis before operation. In 1925 Putman published a paper describing cases contributed by various surgeons in America and since then many cases have been recorded.

Cases of sub-dural hæmatoma are uncommon, but can hardly be called rare. I shall base my remarks on six cases. I have seen three instances of the condition within twelve months and the other three are from the records of the National Hospital.

The pathology is not clear. The source of the bleeding has rarely been determined, but the surmise that it results from tearing of one of the small veins passing from the surface of the brain to the dura, is the most satisfying. It probably results from a sudden dislocation of the brain within the cranium, such as must be caused by a blow on the forehead or on the occiput. The hæmatoma evidently enlarges gradually and by the time it causes symptoms it usually extends over a large part of

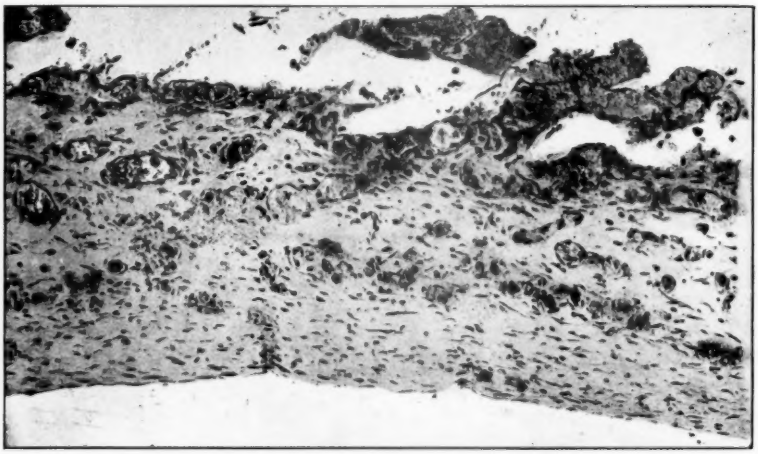


FIG. 2.—Section of the membrane forming the surface of the hæmatoma towards the arachnoid. Note the large number of blood-vessels and thin-walled blood spaces.

one cerebral hemisphere. Most often it lies over the frontal and parietal lobes. In about forty per cent. of cases—chiefly, I think, in the elderly subjects—it is bilateral. The blood may be partly clotted, but a large part of it is nearly always fluid, even in hæmatomata of long standing. Dandy says that if it is aspirated and put in a sterile flask, it remains for weeks without clotting. It seems probable that it is defibrinated as a result of the movement transmitted to it by the pulsation of the brain.

The blood is enclosed by two membranes, one lying towards the dura and attached to the dura, the other lying on the arachnoid, but only very lightly, if at all, attached to it. These membranes are, in themselves, of great interest. They consist of fibrous tissue with very numerous blood-vessels and blood spaces (fig. 2). That towards the dura is thicker and is composed of more dense tissue than that towards the arachnoid. In both membranes the blood-vessels and spaces are in most cases crammed with blood-cells, and these vessels and spaces evidently contain blood belonging to the general circulation. It seems inevitable that they must bleed from time to time and so help to increase the hæmatoma. [A slide was shown illustrating

a hæmorrhage into one of the membranes.] On looking at sections of these membranes one can understand that it was one of the controversies of last century whether the hæmorrhage came before the membrane or the membrane came before the hæmorrhage; Virchow maintained that the membrane resulted from the organization of an inflammatory exudate on the dura and the bleeding occurring into it. Bleeding from these membranes may help to increase the hæmatoma, but on the other hand, absorption of the extravasated blood by these very vascular membranes is going on actively (as is shown by sections stained with Prussian blue), and one feels that in some cases the absorption must win. It is certain that, after operations, hæmorrhage in the sub-dural space is absorbed, but evidence of spontaneous cure of sub-dural hæmatoma is almost entirely lacking. A case has recently been described in which a hæmatoma with a calcified shell was found within the skull of a boy, aged 11 years, and was successfully removed by operation.

As the hæmatoma enlarges, the brain at first adapts itself to it, and during that time there are no symptoms, but eventually the brain beneath the hæmatoma is either compressed or collapses as a result of the constant local pressure,—(there is little rise of *general* intracranial pressure)—and to this local cerebral compression the symptoms of the later stages of the condition must be attributed.

[Slides were shown illustrating the deformity of the brain resulting from local compression in two cases of sub-dural hæmatoma; in both cases the hæmatoma had been bilateral.]

Five of the six patients to whom I refer were males, and it would appear from the literature that this is about the usual sex proportion. In all the cases of chronic sub-dural hæmatoma that Trotter described in his original paper, there was a history of trauma, and trauma has been universally accepted as the exciting cause. Trauma, however, is not the only factor in the causation; the part played by age—and all that word implies—and also by other causes of degeneration is worthy of notice. Sub-dural hæmatoma is met with in subjects of all ages, but it is very much more common after the age of 40, though most men by that time have given up motor-cycling and Rugby football. A review of published cases shows that in the younger subjects there is nearly always a history of a severe blow on the head, sufficient to render the patient unconscious, but in subjects over 50 the trauma is often trivial and no history of it may be obtained.

In a woman aged 44, the condition resulted from a severe fall from a step-ladder, the back of her head striking a shop counter as she fell; she was rendered unconscious. In the other five cases, the patients were over 50; in only one of them was there a history of a blow of any considerable severity, and none of them was unconscious. In one case, minute questioning of the patient and his wife and daughter, failed to elicit any history of a blow or fall; in another case also no history of trauma was given in the hospital notes; the remaining two patients, a man aged 50 and a man aged 69, had falls in the street without any head injury. Similar cases with trivial injury in elderly subjects have been recorded by Trotter, Cushing and many others. Alcoholism was recognized as a determining factor of pachymeningitis hæmorrhagica and probably should be given a place among the subsidiary predisposing causes of sub-dural hæmatoma. It was present in at least one of my cases and is mentioned in one of Trotter's cases.

In three of my cases in which the trauma was least, or was not discoverable, hæmatomas were present in both sides of the brain. In those with more definite accidents it was unilateral. My very incomplete review of the literature confirms my impression that the bilateral hæmatomas are most often found in subjects over 50, and often in those who have sustained only slight trauma.

I think it would be fair to express the determining cause of sub-dural hæmatoma as trauma *plus* age; the less the patient's age, the more severe, speaking generally, is the trauma acquired, and vice versa. (This does not apply to young children.)

The *clinical course* of cases of sub-dural hæmatoma falls naturally into two stages, the *latent period* and the *period of symptoms*. Speaking in a very general way the latent period seems to be shorter the more severe the trauma. In both my cases with rather severe accidents some symptoms were present from the time of the injury, so that strictly speaking there was no latent period. This was so in the case of the woman aged 44 to which I have already referred. From the time of the accident she suffered from mental confusion, impairment of memory, headaches and even occasional vomiting. Acute symptoms came on about eighteen days after the injury and rapidly led to coma. She was admitted to the National Hospital on the twenty-first day, under the care of one of my colleagues. The next morning a large sub-dural hæmorrhage on the right side was evacuated and the left side of the skull was also explored. Unfortunately the patient did not recover from her comatose state and died 48 hours later.

The other case was that of a man aged 52 whom I saw 9 months ago. Mental dulness and inertia and some difficulty in speech had been present, though varying in degree, since a fall three weeks earlier. This patient was also operated upon and the hæmatoma was evacuated; he made an immediate recovery, and has had no further symptoms.

The length of the latent period is most commonly to be measured in weeks. Three or four months is, however, not uncommon, and a few cases have been recorded in which it exceeded a year. In a case recently shown to this Section by Sir James Purves-Stewart the interval was six years.

Symptoms, when they come on, are of a general character, the most constant and prominent being drowsiness, mental changes and headache. These lead gradually to coma. Focal symptoms, if they occur at all, are late and of a very partial character. Ocular signs, such as pupil changes, diplopia and slight ptosis are common, and usually precede the signs of cerebral palsy. Those are the main outlines of the clinical picture, of which the following case is an interesting and unfortunate example:—

I was rung up by the wife of a medical man, who seemed very agitated about her husband, but when I went to see him about four hours later, I could not for some time understand the cause of her concern. The patient, a man aged 52, was sitting up in bed, and he gave me what seemed a perfectly clear account of his symptoms. He said that he had been having headaches for about ten days, mostly in the morning and evening, and he told me what steps he had taken to try to discover their cause. He had tested his urine several times; he had had a Wassermann test carried out; he had been to an ophthalmologist, and had gone to a nose and throat specialist and had his sinuses examined. He thought that the only causes he had not excluded were too awful to contemplate. I examined him and found not the slightest abnormal physical sign, either in the central nervous system or elsewhere. The blood-pressure was normal—130 mm. Hg—though the vessels were moderately thickened. The pulse-rate was normal—about 70. We talked for three-quarters of an hour, he doing most of the talking. For some time he had not felt really well; had been more easily tired and found it necessary to take a stimulant if he had a call in the evening. He carried on the conversation quite intelligently and normally, except that he went all over the steps he had taken to find the cause of his headaches, at least twice, and was starting again a third time when I made my excuses for departure. As he talked he occasionally rubbed his nose meditatively, and once or twice he yawned slightly. Afterwards his wife told me that his headaches seemed very severe: they seemed to make him go to sleep, and sometimes she had been unable to rouse him: she thought he was unconscious. For ten days or so the headaches had been worse and he had remained in bed, but he had had them for five or six months, and during that time

he had been becoming gradually less active and more drowsy. He used to sleep late in the morning and waken with a headache. He used to lie for a long time, perhaps an hour, in his bath, while patients were waiting in his surgery downstairs, and he said it eased his headache to lie with the back of his head in the water. Later, in a nursing home, where he was well known, I learned that when he had conducted a confinement case there four months previously, the matron and sister had noticed a change in him, they thought he was "a bit vague" was "getting old." When I asked his wife whether it was usual for him to repeat himself in conversation she said he had done that for a long time, and she put it down to oncoming old age. At times, too, he would keep asking the same question over and over again. For some months past his memory had been failing, and he had become very inattentive to his practice. The patient himself not only did not remember the duration of his symptoms, but he could not tell exactly when he had had the various special examinations made. He was usually at his best during the afternoon and was then free from headache and quite clear mentally.

Two days later the repetition in conversation was a little more marked and the patient told me he had seen double a little. He was moved to a nursing home for investigation, and on the third day a lumbar puncture was made in the evening. The spinal fluid pressure was unusually low—60-80 mm. of fluid.

Dr. Greenfield's subsequent analysis of the fluid showed a rise of protein to 0·1%, three cells per c.mm. and negative Wassermann reaction. The fluid was quite colourless.

The blood-pressure, taken that evening, was unusually low—not more than 110, and the pulse-rate was 60.

Next day the patient remained relatively well, though very inert, until the evening. About nine o'clock he fell asleep and before eleven it was found that he could not be roused. About midnight, I saw him with one of my senior colleagues. He was then stuporose, but could be roused and gave some mumbling responses when stimulated. As the examination progressed he wakened up a little more.

Examination of the nervous system then showed slight weakness on the right side of the face. The right arm when held up fell away quickly. The right abdominal reflexes were a little less than the left. Both plantar responses were flexor. When roused, the patient said he saw double and he kept the right eye closed to obviate the diplopia. We considered that he had a frontal, or possibly a callosal tumour. In the course of the next week he remained in a stuporose condition most of the time, but slow answers could usually be obtained from him. The pulse was always from 50-60 per minute. He complained occasionally of pain in the left leg and towards the end of the week weakness in this leg became definite and the plantar reflex became extensor. There was no swelling of the optic discs or even any fullness of the veins. The blood-pressure remained consistently at 110 or a little less. The patient became unconscious on the morning of the eleventh day after I had first seen him and died that evening.

In this case *no history of injury* whatever could be obtained, and I feel that we must learn to diagnose these cases without having any such history to help us. In patients over 50 the trauma is often so slight and so remote that the history of it is hardly to be expected. *The mental changes, drowsiness and headache* are of constant occurrence and are to be regarded as symptoms of a rather wide-spread and not very severe local compression of the cerebral hemispheres. *The mental changes* usually come on more quickly then in the case I have detailed and within a few days the patient may pass into a condition closely resembling senile dementia. The *drowsiness* and *headache* are subject to great variability and if there is any suspicion of sub-dural hæmatoma, one should make a point of seeing the patient a second time after an interval of five or six hours. In at least two of my patients the symptoms have been very much less during the afternoon and most severe in the morning. This variable drowsiness I regard as the most helpful sign.

A similar drowsiness is common in cases of frontal tumour and especially of tumours affecting the anterior part of the corpus callosum, but in such cases it is seldom so variable apart from treatment and it is not likely to be so rapid in its progress. I should like to make it quite clear that these symptoms, headache, mental changes, drowsiness (and later coma)—are the result of *local* cerebral compression and that signs of *general* intracranial pressure are usually absent. In three of my cases in which the spinal fluid was measured, the maximum pressure was found to be 80, 150, and 180 mm. of fluid. Papillœdema has, however, been recorded quite frequently, especially in rather acute cases of sub-dural hæmatoma, and vomiting is not very uncommon; slowness of the pulse is unusual until a late stage. *Slight ocular disturbances* come next in order of time; they are recorded in about half the cases and are very varied. *Focal signs* of cerebral disease, as has been said, usually make their appearance rather late, and are usually slight in degree. They are practically always motor paralytic signs but in a few cases twitching of one side of the face or of one arm has been described. Sensory defect symptoms are less common than motor; one of my patients in whom hæmatomata were afterwards found over both occipital lobes had homonymous hemianopia affecting the left halves of the visual fields.

The *cerebrospinal fluid* is nearly always normal. In one of my patients it showed a distinct increase in the amount of protein and in a number of cases—not more than one-eighth of those recorded—the fluid has been yellow. As these cases have mostly had a history of rather severe trauma, it seems likely that the yellow coloration may result from slight sub-arachnoid hæmorrhage occurring at the time of injury. The *urine* in about ten per cent. of the cases contained albumin; this feature has sometimes led to the condition being mistaken for uræmia. The *blood-pressure* in all my cases has been low and this appears to be a common finding. In one of my patients it rose 25 mm. Hg within a few hours after operation and the higher level was thereafter maintained.

I have come to the conclusion that if sub-dural hæmatoma is suspected, exploratory trephining should be done; others have advocated making a small hole in the skull with a burr and exploring the sub-dural space merely with a needle. If focal signs are lacking, the side on which the hæmatoma lies may be determined by ventriculography, as the effect of the hæmatoma is to push the brain over to the opposite side and usually to cause a reduction in size of the ventricle on the side on which it lies. Dandy goes so far as to say that the diagnosis can always be made by ventriculography. Encephalography by injection of air into the sub-arachnoid space through the lumbar theca, as described by Penfield, is likely to be at least as helpful for diagnostic purposes. I have, however, no personal experience of either of these methods.

Treatment consists in evacuation of the hæmatoma. Usually a rather large bony opening is to be recommended because in a number of cases œdema of the brain has come on a few hours after operation, and has given rise to very severe and alarming symptoms. In most cases, however, recovery seems to be immediate. If signs of œdema occur, hypertonic saline should be given intravenously but it may be necessary to reopen the skull, and in occasional cases it has been found that the hæmatoma had to some extent filled up again. In spite of these difficulties the percentage of recoveries in cases that have been operated on before they had reached a stage of deep coma, is high. Recovery may take a week or two but it always seems to be complete. It will be apparent that even on the surgical side these cases are sometimes beset with difficulty. For all departments, pathological, medical and surgical, they present difficulties and problems, but the problem that is most urgent is that of diagnosis. There must be few conditions of which the pathology is so gross, for which our diagnostic criteria are so inadequate, yet which offer to diagnosis such an ample reward.

The Ætiology of Disseminate Sclerosis: Some criticisms of recent work, especially with regard to the "Spherula Insularis."[1]

By E. Arnold Carmichael, F.R.C.P.Ed.

In the early part of 1930 several papers [1] were published by Miss K. Chevassut and others, working at the Westminster Hospital, on the ætiology and treatment of disseminate sclerosis. Claims were made that a virus, named "spherula insularis," could be obtained and cultured from the cerebrospinal fluid of cases of disseminate sclerosis, and in support figures were quoted demonstrating a change in the pH values of positive cultures: besides such claims, attention was drawn to changes in the Lange gold-sol curves of the cerebrospinal fluid and to dysfunction of the liver as measured by certain tests. I now wish to place before you certain facts relevant to to this work, which are in main the results of an attempt to repeat the work under strictly controlled conditions.

In order to make this paper clearer, the matter will be divided into four main parts, namely:—

(1) The Lange gold-sol curve.
(2) The lævulose tolerance test.
(3) The variation in the pH of cultures.
(4) The microscopic appearance of cultures.

(1) *Lange gold-sol curves.*—Those who work with cerebrospinal fluid and the tests associated with it recognize that the sensitivity of various batches of gold-sol solution vary greatly; and that it is possible to prepare a solution which will precipitate completely in every dilution with normal cerebrospinal fluid. To avoid such variations in sensitivity methods of standardization have been introduced, and in the work published last year on disseminate sclerosis Novick's method of standardization was adopted. Even this method has its limitations, as the following figures show. Three batches of gold-sol solution were made, using the method adopted at Westminster Hospital and standardized according to Novick's method, and were then put up with suitable dilutions of the same cerebrospinal fluid.

	C. arthritis	Disseminate sclerosis
First solution	0012332100/0	1234443200/0
Second solution	0001111000/0	0013344442/0
Third solution	0000110000/0	0012331100/0

These figures point to a difficulty in the standardization of fluids by this method.

For comparison, however, with the Westminster Hospital work, a series of Lange gold-sol curves obtained at the National Hospital by Dr. Greenfield was investigated. The notes of the cases were first carefully examined and only undoubted clinical cases of disseminate sclerosis accepted, namely those with a typical history of eye symptoms, relapses, and double extensor plantar responses. Also, all cases with a history commencing after the age of 40 years were discarded. The chosen cases were then grouped into three series—(1) acute, in which a relapse had occurred within the previous few weeks, (2) progressive, in which the symptoms tended to be steadily progressive, and (3) stationary, in which progress had ceased for a year or more. The gold-sol solution was made according to the method of Mellanby and Davies; several samples were made on each occasion, and only that sample which gave a typical paretic curve with a fluid from an untreated case of general paralysis of the insane was accepted: by this means comparable solutions were obtained. With such solutions, and in these picked cases, the following results were obtained.

[1] This work has been carried out with the aid of a personal grant from the Medical Research Council.

TABLE I.—LANGE GOLD-SOL CURVES.

Colour changes	Acute	Progressive	Stationary
No change	5	7	6
Up to 1, red-blue ...	7	10	6
,, ,, 2, lilac	10	10	3
,, ,, 3, blue	5	6	3
,, ,, 4, grey-blue ...	3	4	—
,, ,, 5, colourless ...	2	6	1
Total ...	32	43	19

No change ...	18	19·2%	68·1%
Up to 2	46	48·9%	
Luetic	18	19·2%	31·9%
Paretic	12	12·7%	

Scrutiny of this table reveals the fact that the character of the curve is in no way associated with the stage of the disease. Secondly, the figures show that in only 31·9% of the ninety-four cases were curves of three and over obtained; this compares with a figure of 54% as published in the work under critical review. It is of interest to recall that Greenfield and Carmichael [2] published the results in two series of cases, in each of which a different method of making the gold-sol solution had been adopted In the first series the formalin method was used, and in the second series the method of Mellanby and Davies. The figures were as follows:—

	Completely negative	Up to 2	Luetic	Paretic
First series: 115 cases ...	6%	63·5%	17·4%	13·1%
Second series: 190 cases ...	6·8%	59·5%	19·5%	14·2%

These figures compare very favourably with the present series, giving a percentage of 30·5 and 33·7 for curves over three. It would thus appear that the workers at the Westminster Hospital, with a 54% of curves over three, may have been using an over-sensitive Lange gold-sol solution.

(2) *Lævulose tolerance tests.*—Two series of cases, all of disseminate sclerosis, were investigated, one at St. Bartholomew's Hospital, where the chemical estimations were under the direction of Dr. E. N. Allott, and the other at the National Hospital, Queen Square, the estimations being controlled by Dr. E. O'Flynn. The lævulose used at both hospitals was obtained from the same firm, and contained approximately the same quantity of impurity, making the content 95% lævulose, if all the impurity was glucose, the estimations of the blood-sugar were made by Hagedorn's method. In a normal individual, on the ingestion of 50 grm. of lævulose, the blood-sugar level does not rise above 30 mgm. in the majority of cases, and it is commonly accepted that a rise above that level may indicate liver dysfunction. In the two series, one of seventeen cases at St. Bartholomew's Hospital, and the other of eleven cases at the National Hospital, only six cases showed a rise of over 30 mgm. in the blood-sugar level. The actual figures are: 3, 5, 10, 11, 13, 15, 17, 17, 19, 20, 20, 21, 21, 23, 23, 25, 25, 25, 25, 27, 29, 30, 35, 35, 37, 38, 48, 75, making a percentage of 21·9 with figures over 30. In one case the woman had just been confined, and this offered a possible explanation for the rise to 37 mgm.; in the other cases no explanation could be found. It is worthy of note, however, that only in two cases did the level rise above 40 mgm., because the workers at the Westminster Hospital exhibited a diagram of four curves with respective rises of 70, 80, 80, and 120 mgm., and suggested that similar curves occurred in 70% of the cases they examined. Such a high percentage of abnormals has not been obtained in the two series reported here, nor were such consistently high levels obtained in those curves that were abnormal. It is possible that the Westminster Hospital workers used less pure lævulose, which might account for the results they obtained; or else arsenical treatment may have been exhibited previous to the test, thereby disturbing normal liver function.

(3) *pH determinations of cultures.*—We now come to the crucial experiments dealing with the characteristics of the cultures and their microscopic appearance. It is fair to assume that few will be willing to estimate the character of an object simply from its microscopic appearance and that bacteriologists will demand some specific change in cultural reactions as criteria of a living organism. Therefore the experiments dealing with pH values assume as much significance as, if not more than, the microscopical experiments. On account of this, very especial care was paid to the following pH determinations, and Dr. Elford, of the National Institute for Medical Research, rendered most valuable aid in criticizing and controlling these results. Several methods of determining the pH were available and require criticism at this stage. Four methods are possible, namely, (1) colorimetric, by means of suitable indicators and a comparator, (2) the quinhydrone method, (3) the method using the bubbling hydrogen electrode, and (4) the method by means of the hydrogen cell electrode of Bailey's type. Indicators are undoubtedly useful and give good results if great accuracy is not required: at most the error may be 0·1 to 0·2 of a pH, but any fall or rise of more than 0·2 is easily discernible: this method has been used as a confirmatory method in the present work. The quinhydrone method is accurate only up to a pH of 7·8, above which level it becomes less accurate: this method was used on occasion, as it is valid, but it was not used generally and never with fluids having a pH higher than 7·8. The bubbling hydrogen electrode offers many technical and theoretical difficulties when one is dealing with biological fluids: this method was not used, because with a similar electrode to that used by the Westminster Hospital workers, no constant estimations of media could be obtained: this was due to the excessive frothing which occurred on bubbling the hydrogen through the albuminous fluid, thus allowing the platinum point to lie above the level of the fluid being tested and to become dry. However, with buffer solutions of a known pH, constant readings were obtainable, as it was possible to saturate the fluid with hydrogen without frothing taking place (the figures for buffer solutions were the same whatever method of estimation was used). Again, if hydrogen is bubbled through a biological fluid, the process of bubbling removes any easily dissociated carbon dioxide from the mixture, rendering it more alkaline. On account of the practical difficulty alone, and quite apart from the theoretical loss of carbon dioxide, this method was considered, after a series of experiments, impracticable and untrustworthy. Lastly, the closed cell method: here there is no possible error arising due to loss of carbon dioxide, and it was found that the results were always strictly comparable in a series of examinations of any one fluid. This method was therefore the method of choice. In all the work on pH estimations careful note as to temperature was taken and corrections made in the readings accordingly. Also, the nature of the case from which the cerebrospinal fluid was obtained was in the majority of cases not known to me until after the pH values had been determined. The Hartley's broth used in these experiments was exactly the same as that used by the workers at the Westminster Hospital, being obtained from the same source. The serum was obtained from the blood of students at St. Bartholomew's Hospital, who willingly volunteered for the work. The serum was used within from 24 to 72 hours of obtaining the blood, and was filtered by negative pressure through a Seitz filter. The proportions of Hartley's broth, serum, and cerebrospinal fluid used, were the quantities advised by Miss Chevassut in her paper or in personal communications to me. The experiments dealing with pH values covered much ground, and were frequently repeated to avoid any possible error. They may be conveniently divided into four groups: the determination of (i) the pH values of various mixtures of broth and serum, (ii) the pH values of broth and serum over a period of days, (iii) the pH values of broth and serum and normal cerebrospinal fluid, or cerebrospinal fluid from cases other than disseminate sclerosis, and (iv) the pH values of broth and serum and cerebrospinal fluid from cases of disseminate sclerosis.

(i) pH values of broth and serum.—The pH value of serum was found to differ in various samples of serum from different individuals, and no constant level was obtained. The following table demonstrates the variation in several sera before and after filtration with different filters. In most the pH was above 8·0.

TABLE II.—pH OF SERUM BEFORE AND AFTER FILTRATION. (TWENTY-FOUR HOURS AFTER WITHDRAWAL).

No.	Before	Filter	After
1	8·0	L3	8·2
2	8·1	L3	8·3
3	7·9	Berkefeld	8·4
4	7·8	Berkefeld	8·7
5	8·1	Mandler	8·6
6	8·0	Seitz	8·4
7	7·9	L2	8·4

With such variation in the pH value of serum, it is obvious that the addition of such serum to Hartley's broth in constant proportions would give different pH values of the resultant mixture. Figures to demonstrate this are tabulated below:—

TABLE III.—pH READINGS OF SERUM AND BROTH AND OF VARIOUS MIXTURES.

Serum	Broth	Proportions	Mixture
8·01	7·18	B. 10 cc. S. 3 cc.	7·3
8·4	7·2	B. 10 cc. S. 3 cc.	7·6
8·7	7·3	B. 10 cc. S. 3 cc.	7·5
8·5	7·3	B. 9 cc. S. 3 cc.	7·5
8·4	7·3	B. 10 cc. S. 3 cc.	7·6
8·2	7·3	B. 8 cc. S. 3 cc.	7·53
8·2	7·3	B. 10 cc. S. 3 cc.	7·46
8·2	7·3	B. 12 cc. S. 3 cc.	7·44
8·2	7·3	B. 15 cc. S. 3 cc.	7·37
8·4	7·4	B. 10 cc. S. 3 cc.	7·9
8·6	7·4	B. 10 cc. S. 3 cc.	7·7
8·4	7·6	B. 8 cc. S. 3 cc.	7·8

These figures also demonstrate that by altering the ratio of broth to serum variation in the pH values of the mixture resulted. Difficulty was therefore encountered in obtaining a mixture on every occasion with the pH of 7·5 to 7·6 as is stated to be required in the publications of last year. Possible solutions of this difficulty offered themselves: the resultant mixture could be titrated with decinormal acid or alkali to the required pH. This was in effect done, and cerebrospinal fluid added; but the previous workers were averse to this method, so a large series of experiments with mixtures of varying pH values to which cerebrospinal fluid was added were carried out. Results in both instances will be dealt with later.

(ii)—pH values of broth and serum over a period of days. The statement was made in the work from Westminster Hospital that, if a mixture of broth and serum with a pH of 7·6 was kept over a period of days, the pH value remained more or less stationary, or became slightly acid: the following figures were quoted:—

Days	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Broth and serum	7·6	7·5	7·4	7·4	—	7·4	7·4	—	—	7·5	—	7·5	7·4	—

Repetition of these figures proved impossible when the serum used was fresh: this is well demonstrated by the following figures:—

TABLE IV.—pH READINGS OF BROTH AND SERUM.

Proportions B.	S.	Same day	1	2	3	4	5	6	7	8	9	10	11	12	13	14
8	3	7·53	—	—	—	—	—	—	8·2	—	—	—	—	—	—	8·1
10	3	7·4	7·6	—	—	—	7·7									
10	3	7·5	—	—	—	7·7										
10	3	7·3	—	—	7·57											
10	3	—	7·6	—	—	—	—	7·7								
12	3	7·44	—	—	—	—	—	—	7·95	—	—	—	—	—	—	7·97
15	3	7·37	—	—	—	—	—	—	7·88	—	—	—	—	—	—	7·88

In all cases the mixture of broth and serum became more alkaline; this change to the alkaline side is explicable on the loss of the less easily dissociated carbon dioxide which comes off slowly over a period of days.

(iii) pH values of broth and serum and normal cerebrospinal fluid, or cerebrospinal fluid from cases other than disseminate sclerosis.—To mixtures of broth and serum with pH values varying between 7·4 and 7·6, cerebrospinal fluid was added and pH determinations made of the complete mixture. The cerebrospinal fluid was obtained from patients suffering from diseases other than those involving the central nervous system, or from diseases clinically not disseminate sclerosis. The diagnosis of these cases lay in the hands of Professor Fraser at St. Bartholomew's Hospital and my colleagues at the National Hospital, Queen Square. The results obtained in these experiments are as follows:—

TABLE V.

pH of broth and serum	Case No.	Disease	C.S.F. added	Same day	pH readings of cultures. Days after puncture 1	2	3	4	5	6	7	8	9	
7·4	34	Amyotrophic lateral sclerosis	5 c.c.	—	7·7	7·8	8·4	—	—	--	—	—	—	HE
					7·8	7·8	8·2							C
7·4	32	Gastric ulcer	,,		8·0	—	—	—	7·9	—	—	—	—	HE
					8·0				8·0					C
7·4	33	Normal	6 c.c.	—	7·9	—	—	—	7·9	—	—	—	—	HE
					7·9				7·9					C
7·5	18	Neurasthenia	5 c.c.	7·5	8·0	7·9	8·2	—	—	—	—	—	—	HE
				7·7	8·0	8·0	8·2							C
7·5	19	General paralysis	,,	7·6	8·0	8·0	8·2	—	—	—	—	—	—	HE
				7·6	8·0	8·0	8·2							C
7·6	16	Cerebral tumour	,,	—	—	—	7·9	8·2	—	—	—	—	—	HE
							8·1	8·2						C
7·6	17	Peripheral neuritis	,,	—	8·1	8·0	—	8·4	—	—	—	—	—	HE
					8·2	8·0		8·4						C
7·6	25	Normal	,,	—	8·3	—	—	—	—	8·3	—	—	—	HE
					8·4					8·4				C
7·6	26	,,	,,	—	8·3	—	—	—	—	8·3	—	—	—	HE
					8·4					8·4				C
7·6	27	,,	,,	—	8·3	—	—	—	—	8·4	—	—	—	HE
					8·4					8·4				C
7·6	28	,,	,,	—	8·2	—	—	—	—	8·2	—	—	—	HE
					8·4					8·4				C
7·6	29	,,	,,	—	8·1	—	—	—	—	8·3	—	—	—	HE
					8·2					8·2				C
7·6	30	,,	,,	—	—	8·2	—	—	—	—	7·9	—	—	HE
						8·2					8·0			C
7·6	31	,,	,,	—	—	8·4	—	—	—	—	8·1	—	—	HE
						8·4					8·2			C

HE = hydrogen electrode. C = comparator.

In every instance the pH of the resultant mixture rose to the alkaline side, reaching a level of 8·0 or more. These figures do not tally with those previously published, quoted hereunder:—

Days	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Broth and serum and normal c.s.f.	7·6	7·5	7·5	7·5	—	—	—	7·5	—	—	7·5	—	7·6	7·5

There is thus a large discrepancy between the figures published from the Westminster Hospital and those reported upon in this paper. The reason for the shift of the pH values to the alkaline side was also investigated, and will be dc with later.

(iv) pH values of broth and serum and cerebrospinal fluid from cases of disseminate sclerosis.

A similar series of observations were made with mixtures of broth and serum to which cerebrospinal fluid from cases of disseminate sclerosis was added. In all respects analogous results were found as with cerebrospinal fluid from normal cases. The results are drawn up in Table VI.

TABLE VI.—DISSEMINATE SCLEROSIS.

pH of broth and serum	Case No.	C.S.F. added	Same day	pH readings of cultures. Days after puncture 2	3	4	5	6	7	8	9	10	
7·3	22	5 c.c.	—	—	—	—	—	—	—	—	—	—	HE
				7·8	8·3								C
7·4	37	,,	7·7	7·9	—	—	8·3	—	—	—	—	—	HE
			7·8	7·8			8·4						C
7·4	36	,,	7·7	7·8	—	—	8·4	—	—	—	—	—	HE
			7·8	7·9			8·4						C
7·4	35	,,	7·7	7·9	—	—	8·4	—	—	—	—	—	HE
			7·8	7·9			8·4						C
7·4	21	,,	—	7·9	—	8·0	—	—	—	—	—	—	HE
				8·0		8·0							C
7·4	14	,,	—	—	—	—	—	—	—	—	—	—	HE
				7·9	8·4	8·4							C
7·4	15	,,	—	—	—	—	—	—	—	—	—	—	HE
			7·9	8·3		8·3	8·4		8·4	8·4			C
7·4	56	,,	—	—	—	—	8·4	—	—	—	—	—	HE
7·4	57	,,	—	—	—	—	8·4	—	—	—	—	—	HE
7·5	20	,,	7·3	8·1	8·2	8·2	—	—	—	—	—	—	HE
			7·6	8·2	8·2								C
7·6	A1	,,	—	7·8	8·2	8·2	—	—	—	—	—	—	C
					8·3								HE
7·6	A2	,,	—	7·7	8·2	8·2	—	—	—	—	—	—	C
7·6	44	,,	—	—	—	—	8·41	—	—	—	—	—	HE
				7·9	8·0	8·2							C
7·6	52	,,	—	8·0	—	8·2	—	—	—	—	—	—	C
7·6	53	,,	—	—	—	—	8·3	—	—	—	—	—	HE
				8·0		8·2							
7·6	54	,,	—	—	—	—	8·3	—	—	—	—	—	HE
					8·2								C
7·7	55	,,	—	—	—	—	—	—	—	8·3	—	—	HE
				8·3									C
7·7	30	,,	—	7·9	8·2	—	—	—	—	—	—	—	HE
				8·1	8·4								C
7·7	31	,,	—	8·1	—	—	—	—	—	—	—	—	HE
				8·2									C

Scrutiny of this table shows that in every instance, nineteen cases in all, composed of acute, progressive and stationary types, the resultant mixture became alkaline. Thus in this series no confirmation was established of the shift to the acid side, as claimed by the workers at the Westminster Hospital; in fact the direct opposite was observed in every instance. The following figures were quoted in the work of last year.

Days	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Broth, serum,	7·6	7·4	7·2	7·0	6·9	7·1	7·25	7·4	7·5	7·6	7·8	8·0	8·0	8·0
and c.s.f.	7·6	7·5	7·3	7·1	7·0	6·9	7·1	7·25	7·4	7·6	7·7	7·8	7·8	7·8
(Diss. scler.)	7·5	7·4	7·3	7·2	7·1	7·02	6·89	7·1	7·2	7·4	7·5	7·6	7·8	7·9

Again, with a mixture of broth and serum titrated to a standard pH of **7·6**, the addition of cerebrospinal fluid causes the pH to shift to the alkaline side.

TABLE VII.

pH Hartley's Broth, 10 c.c. Human Serum 3 c.c. (titrated)	Case No.	Disease	Quantity of C.S.F. added	pH readings of fluid culture. Days after puncture. 1	2	3	4	5	6	7	8	9	10
7·6 (QH)	1	Gastric ulcer	7 c.c.	7·8 (C)	8·0 (C)	8·1 (C) 8·1 (HE)	8·1 (C)	8·1 (C)	8·1 (C)				
,,	2	Gastric ulcer	7 c.c.	7·9 (C)	8·0 (C)	8·0 (C)	8·1 (C)	8·1 (C)	8·1 (C)	8·1 (C)			
,,	5	Disseminate sclerosis	7 c.c.	7·8 (C)	8·0 (C)	7·9 (C)	8·0 (C)	8·0 (C)	8·1 (C) 8·2 (HE)	8·1 (C)			
,,	4	Disseminate sclerosis	7 c.c.	7·8 (C)	7·9 (C)	8·0 (C) 8·1 (HE)	8·1 (C)	8·0 (C)	8·0 (C)	8·0 (C)	—	—	8·5 (HE)
,,	3	Disseminate sclerosis	7 c.c.	7·8 (C)	8·0 (C)	8·0 (C)	8·0 (C)						
Control.	No. C.S.F. added			7·6 (HE)	7·6 (C)	7·6 (C)	7·65 (HE)						

QH = Quinhydrone. C = Comparator. HE = Hydrogen electrode.

Thus, no matter how the mixture of broth and serum was prepared, in every case, irrespective of the source of the cerebrospinal fluid, the pH of the mixture after the addition of cerebrospinal fluid became more alkaline.

Experiments were then carried out to ascertain the cause of this shift of the pH to the alkaline side. Firstly, the quantity of the carbon dioxide in a fresh specimen of broth and serum and cerebrospinal fluid was measured, and again four days later, with the following results :—

		Immediately after addition		Four days later, after exposure under aerobic conditions
Carbon dioxide content of mixture of broth, serum and c.s.f.	Case I ...	25·2 volumes %	...	19·3 volumes %
	Case II ...	16·2 volumes %	...	5·9 volumes %

These figures demonstrate that a very considerable loss of carbon dioxide takes place, which will render the mixture more alkaline. Again, if the loss of carbon dioxide is retarded by culturing under paraffin, a shift to the alkaline side is less evident, as demonstrated by these figures.

TABLE VIII.

UNDER PARAFFIN.

pH Hartley's broth, 10 c.c. Human serum (titrated). 3 c.c.	Case No.	Disease	Quantity of C.S.F. added		pH readings of fluid culture. Days after puncture 1	2	3	4	5	6	7	8	9	10
7·6	7	Diabetes mellitus	5 c.c.	C	7·5	7·5	7·5	7·6	7·6	7·7				
				QH	—	7·6	7·6	—	—	7·7				
7·6	13	Subacute combined degeneration	,,	C	—	7·6	—	—	7·8	—	7·8			
				QH	—	—	7·8	—	—	—	—	7·8		
7·6	8	Disseminate sclerosis	,,	C	7·5	7·5	—	7·6						
				QH	—	7·6	7·6							
7·6	12	,,	,,	C	—	7·6	—	—	7·8	—	7·8			
				QH	—	—	7·7	—	—	—	—	7·8		
7·6	10	,,	,,	C	—	7·6	—	—	7·8	—	7·8			
				QH	—	—	7·7	—	—	—	—	7·8		
7·6	11	,,	,,	C	-	7·6	—	—	7·8	—	7·8			
				QH	—	—	7·8	—	—	—	—	7·8		
7·6	Control		No C.S.F. added	C	—	7·6	—	—	7·6	—	7·6			
				QH	—	—	7·6	—	—	—	—	7·6		

QH = Quinhydrone. C = Comparator.

Again, if the lost carbon dioxide is replaced by placing the mixture in a partial pressure of carbon dioxide, equal to that of the alveolar air (approximately 6%), the pH values move to the acid side, only to return to the alkaline side after exposure to the ordinary atmosphere. The following figures illustrate this fact :—

pH of mixture two days old	8·0
pH of mixture after two days in 6% carbon dioxide ...	7·4
pH of mixture after exposure to air for two days ...	7·9

It is therefore apparent that the alteration of the pH to the alkaline side is due to a loss of carbon dioxide, and that unless care is taken to avoid this loss, it is impossible to prevent the alteration of the pH of the mixture to the alkaline side after the addition of the cerebrospinal fluid. As such precautions were not adopted by the workers at the Westminster Hospital, it is impossible to explain or repeat the figures they obtained for controls, or for cultures of cerebrospinal fluid, using aerobic methods of cultivation. These experiments have resulted in an absolute failure to reproduce the figures quoted in the paper published at the beginning of last year for broth and serum, and for broth and serum and normal cerebrospinal fluid, and for broth and serum and disseminate sclerosis cerebrospinal fluid.

(4) *The microscopic appearance of cultures.*—In this work Mr. Barnard has generously rendered assistance by supplying the microscope and by personally examining eight cultures from cases of disseminate sclerosis.

The cultures were prepared according to the method described by Miss Chevassut, and the only criticism suggested regarding the work was that, as some of the work necessitated the carriage of cerebrospinal fluid to Hampstead from various hospitals, the virus might be damaged in transit and thus cause negative cultures. This criticism has been met by repeating the work in Dr. Greenfield's laboratory at the National Hospital, Queen Square, where transit cannot remain a valid criticism.

Irrespective of whether the cerebrospinal fluid has been submitted to transmission across London or not, the microscopic picture of the nineteen cultures of disseminate sclerosis fluid differed in no way from the picture of normal fluids, or of uninoculated material. In all, nineteen fluids from cases of disseminate sclerosis were examined, eleven at Queen Square and eight at Hampstead. Mr. Barnard examined eight cultures of disseminate sclerosis fluids at Queen Square and found nothing distinctive in these cultures.

Summary.—(1) A series of Lange gold-sol curves in ninety-four cases of disseminate sclerosis showed a curve rising above 3 in 31%.

(2) A series of lævulose tolerance tests in twenty-eight cases of disseminate sclerosis showed a rise of over 30 mgm. of blood-sugar in 21·9%.

(3) pH determinations of broth and serum, of broth and serum and normal cerebrospinal fluid, and of broth and serum and disseminate sclerosis cerebrospinal fluid, exhibited a shift to the alkaline side in every instance. This shift was due to a loss of carbon dioxide.

(4) No distinctive spherules were found in nineteen cultures of cerebrospinal fluid from cases of disseminate sclerosis.

There is one more test I should like to mention. The Westminster Hospital workers and myself were supplied with numbered specimens of cerebrospinal fluid which we cultured independently. I cultured a relatively small number, with negative results, while the Westminster Hospital workers cultured 32 samples of fluid. Of these 32 samples, 14 were from cases of disseminate sclerosis, the remaining 18 were from cases other than disseminate sclerosis. In no fluid from cases of disseminate sclerosis were spherules cultured at the Westminster Hospital laboratories, and in the 18 controls one specimen grew spherules, that being a case of chorea.

CONCLUSIONS.—These experiments fail to substantiate the work from the Westminster Hospital claiming the presence of a virus, so-called "spherula insularis," in cultures of cerebrospinal fluid from cases of disseminate sclerosis.

REFERENCES.

[1] "Ætiology of Disseminated Sclerosis," K. Chevassut, *Lancet*, 1930 (i), 552; "Specific Vaccine Treatment in Disseminated Sclerosis," Sir James Purves-Stewart *ib.*, 560. [2] "The Cerebrospinal Fluid in Clinical Diagnosis," J. G. Greenfield and E. A. Carmichael, London, 1925.

Discussion.—Sir JAMES PURVES-STEWART: After considering Dr. Carmichael's paper, it seems to me that a large proportion of his results which are apparently at variance with those of Miss Chevassut are due to his having employed different methods, e.g., a different colloidal-gold solution and a different electrode for determination of the pH.

It is difficult for anyone like myself, without bacteriological or biochemical knowledge, to follow the intricate technicalities amongst which Miss Chevassut and Dr. Carmichael move so easily.

To me, the difference in the gold-curves as recorded by these two observers, seems more apparent than real. Dr. Carmichael, with his particular solution of colloidal gold, gets a positive gold-curve in 80% of his cases, a figure even higher than Miss Chevassut's 77%. There is no serious discrepancy on this point.

We must remember that even a positive gold-curve does not necessarily prove the existence of a living virus. Whatever be the cause of the malady, the gold-curve is probably a concomitant phenomenon. This is shown by the fact that a positive colloidal gold-curve is obtainable in "dead" fluids, i.e., hours after their withdrawal from the body, fluids in which positive cultures of the spherula can no longer be obtained. The gold-reaction, therefore, may only be the result of some toxin resulting from the causal agent of the disease.

Deficiency of metabolic and antitoxic liver functions, if present, indicates a toxic factor. Lævulose tolerance tests are of little value as indicating deficiency of liver function, unless they co-exist with excess of indican in the urine (ten to twelve times the normal, according to Miss Chevassut) and with negative glycuronic acid tests. Neither of these tests was carried out by Dr. Carmichael. All that the lævulose tolerance tests indicate is the possibility of deficient detoxicating power in the liver.

Then we come to the question of alkalinity, in mixtures of Hartley's broth, blood-serum, and cultures of the spherula—the pH reaction. The crucial point of difference between these two observers is as to the type of hydrogen electrode which was employed. Miss Chevassut obtained her results with a bubbling hydrogen electrode, working at a given rate (two bubbles per second), being careful to keep the platinum point below the level of the fluid and so avoiding the possibility of frothing, to which Dr. Carmichael calls attention. Dr. Carmichael, on the other hand, prefers a Bailey's closed-cell electrode, which he believes to be better.

In view of this difference in the electrodes used by the two observers, it is not surprising that they get different results. Dr. Carmichael fails to observe the occurrence of an acid wave as described by Miss Chevassut, using a different form of electrode. The two sets of results are not strictly comparable. It is like comparing a cat with a dog, or a sheep with a goat.

These discrepancies can only be settled by mutual agreement upon methods of observation. If such agreement can be arrived at, similar results ought to be attained by them both.

Lastly, on the question of securing cultures of Miss Chevassut's spherula, Dr. Carmichael has obtained negative results in nineteen successive cases of disseminated sclerosis. Miss Chevassut, on the other hand, secured positive cultures in 93% of her first series of 176 cases, together with uniformly negative results in a control series of 269 cases of other diseases and of other individuals. A further series of 234 cases of disseminated sclerosis has yielded positive results in 89%. Since Miss Chevassut's publication, Smith and Ransom, of Liverpool,[1] have secured positive cultures in nine out of eleven cases, whilst Zerkowitz, of Buda-pest, has also secured positive cultures in twenty-six out of twenty-eight cases of disseminated sclerosis.

Whatever be the nature of the morphological appearances, which Miss Chevassut has repeatedly demonstrated under the ultra-microscope, the fundamental questions, from the clinician's point of view, seem to be as follows: (1) Is this spherula which is seen in cultures of cerebrospinal fluid from disseminated sclerosis, a specific appearance in the disease? (2) Is it a vital phenomenon or merely a biochemical reaction? (3) Are filterable viruses, as

[1] *Lancet*, 1930 (ii), 901.

a class, to be regarded as living organisms or not? (4) Does an experimental vaccine prepared from the spherula (whether it be a vital or a biochemical affair) produce beneficial therapeutic effects, and if so, in what way?

It is evident that the problem calls for further research, and that we have not yet reached the stage of final decision.

Miss K. CHEVASSUT said: It has never been claimed that the gold-curve and lævulose tolerance test are in favour of the contention that a virus has been obtained and successfully cultured, and it is difficult to understand why Dr. Carmichael considers this to be so. I conclude from my results that in disseminated sclerosis there is deficiency in the anti-toxic and metabolic functions of the liver. I quote from my paper published in March:—

> "The question arises whether the ætiological factor is responsible for such loss of detoxicating power, or whether, owing to this deficient detoxicating mechanism, this factor is able to gain access to the body. In either case it seemed probable from these experiments (i.e., liver function tests) that there is a *toxic* factor to be taken into account in disseminated sclerosis, whether this be primary or secondary to some ætiological agent."

As regards the colloidal gold test, again quoting from my paper:

> "Thus it has been found that in all cases of disseminated sclerosis in which the colloidal gold test was positive, the virus could be cultured from a sample of cerebrospinal fluid taken simultaneously. If, on a subsequent occasion, a sample of cerebrospinal fluid from the same patient yielded negative cultures the gold-curve had also become negative. This observation was confirmed so often that it must be concluded that there is some relationship between the factor responsible for the precipitation of colloidal gold and the presence of the virus in cultures of cerebrospinal fluid. It is evident that this factor cannot possibly be related directly to the presence of the virus. Cerebrospinal fluid will of course precipitate colloidal gold many hours after withdrawal, when it can no longer be used to obtain cultures of the virus. Neither is the converse relationship necessarily true, for the gold test may be negative in cerebrospinal fluid from which positive cultures can be obtained. Hence, although a correlation of the colloidal gold reaction and cultural results shows a definite connection in this respect, the precise relationship has not been determined. It is conceivable that factor responsible for precipitation of the gold results from some product, toxin or otherwise, of the virus. This possibility will be investigated in future research."

Gold-curve.—(1) How does Dr. Carmichael prepare a solution of colloidal gold, which will precipitate completely in every dilution with normal cerebrospinal fluid? (2) Has he prepared any gold by the method described in the publication, or is it by the method of Mellanby and Davies that he gets this solution?

Method of standardization.—The foundation of the colloidal-gold test was laid by Zsigmondy, who used it as a means of quantitative protein estimation. He determined the gold factor for various protein substances, i.e., the number of milligrammes of protein, just sufficient to prevent precipitation of a definite quantity of colloidal gold in the presence of a known quantity of a certain percentage of electrolyte (sodium chloride). Depending upon the nature and concentration of the electrolyte present, various alterations of the original dispersion phase of the gold solution may be produced, manifested by a range of colours. Zsigmondy found that the degree of protection is specific for each protein examined and may be expressed in terms of milligrammes of protein capable of protecting 5 c.c. of a gold solution against a known quantity of sodium chloride. In other words, under the same conditions a given quantity of protein will regularly prevent a given quantity of *electrolyte* from precipitating a given quantity of colloidal-gold solution.

Thus the precipitation by an electrolyte is the fundamental chemical basis of the colloidal-gold work, and appears to be the only scientific and chemically accurate method of standardization. This precipitation of the colloidal gold by an electrolyte is the underlying principle of Novick's method, which was employed for standardization in my work. In my publication of March 15 it is pointed out that the standard adopted is as follows: "5 c.c. of the colloidal-gold solution should be completely precipitated in one hour by 1·7 c.c. of a 1% solution of sodium chloride." This was employed as advised in the paper on "The Value and Mechanism of the Colloidal Gold Test," by Dr. John Cruickshank (*Brit. Journ. Ex. Path.*, 1920, i, p. 73), a comprehensive treatise on the gold test.

In addition, the various samples of gold used in experiments described in the publication were all tested with normal cerebrospinal fluids, though this was considered secondary in importance to the physico-chemical precipitation test.

The method of preparation of gold used at Westminster Hospital is that originally described by Lange. This was adopted for three reasons: (1) It was the method used in the Westminster Hospital Pathological Laboratories for many years, so that for purposes of comparison it was thought advisable to keep to the method. (2) It was thought best to use the method (formalin and potassium carbonate and gold chloride) described originally by Lange; and (3) it was found that the method gave perfectly reliable and constant results, if carried out precisely according to the instructions in the publication of March 15, and satisfying the criteria laid down therein.

Dr. Carmichael states that he gets practically the same results with the method of Mellanby and Davies as in his former work with Greenfield, when he used the formalin method. Does he mean by this, Lange's original method, and if so, why does he now imply that he considers the formalin method unreliable?

Dr. Carmichael's observations on the curve in relation to the stage of the disease confirm our own observation, for, as pointed out by Sir James Purves-Stewart, in ordinary spontaneous remissions occurring in the course of the disease we have invariably found the gold-curve to be positive just as Dr. Carmichael has found in his stationary cases. This observation gave rise to Sir James's conclusion that the remission or arrest of the disease (including cases in statu quo, i.e., stationary) consequent upon experimental vaccine treatment was a totally different affair from the ordinary spontaneous remissions. In the latter type of case, as Dr. Carmichael mentions, a positive gold-curve can still be obtained; in the former type of case, which has become stationary or remitted after experimental vaccine treatment, the gold-curve becomes negative, as pointed out in Sir James Purves-Stewart's paper (loc. cit.).

With reference to Table I in Dr. Carmichael's paper, the interpretation of the gold-curve, as commonly accepted, surely depends upon the position of the tube or tubes in which precipitation occurs in the series. Thus the various curves are described according to the relationship of their maximal precipitation. Dr. Carmichael does not state where the various colour changes occur in his series. Are they at the beginning or the middle of the curve?

I do not understand why he groups curves marked "No change" and "Up to 2" together.

It is commonly accepted that a paretic curve means that maximal precipitation occurs in the first five dilutions, irrespective of the degree of precipitation. Similarly a luetic curve means that maximal precipitation occurs in tubes 3 and 4 (dilutions 1/40 to 1/80), again irrespective of the degree of precipitation. Hence the phrase "up to 2" or "up to 3" is valueless.

As regards total number of cases giving a positive curve of any sort in disseminated sclerosis:—Dr. Carmichael apparently finds a positive curve in 80·8% (i.e., 48·9% + 19·2% + 12·7%). Ayer and Foster obtained positive curves in 75% of cases.

In my Westminster publication, I stated that a positive curve is obtained in 77% of cases of disseminated sclerosis. This is in harmony with the above percentages quoted.

Dr. Carmichael states that I claim that in 54% of cases, curves over 3 are obtained and described in my publication. I do not understand why he makes this statement. I quote from my paper:—

> "The results showed that in disseminated sclerosis there is one important diagnostic point about the gold-curve revealed by such observation of the tubes—namely, that precipitation almost invariably occurs first in the fourth tube, that is, in the dilution 1/80. Whatever the final reading, this change can usually be observed within an hour of doing the test, although at first the precipitation may be very slight. It was found that in 70 per cent. of these cases giving a positive gold-curve, precipitation occurred in the dilutions 1/80 to 1/640, producing a curve of the type 0003222200. Initial and usually maximal precipitation was manifest in the 1/80 dilution. In certain stages of the disease the cerebrospinal fluid gives a type of curve in which precipitation occurs in the first five or six tubes. *In either case the degree of precipitation is usually not greater than that indicated by the figures 3 or 4.*"

Lævulose tolerance test.—(1) Lævulose used in the tests published from Westminster Hospital was the purest obtainable, the same as used by Dr. Carmichael himself.

(2) The lævulose tolerance tests were carried out in conjunction with the indican and glycuronic acid tests, and it was the correlation of the results of these three tests which led to the conclusion that the detoxicating power of the liver was deficient.

(3) A certain number of cases were tested, using galactose (pure with a rotatory power of 76°); these confirmed the lævulose tolerance test.

In the *Lancet* (1930, i, 659) there is a communication by Dr. A. F. Hurst, dealing with my observations on the functional efficiency of the liver in disseminated sclerosis. He states that his observations confirm mine. This confirmation is of particular value coming, as it does, from such an authority on digestive and liver disturbances.

pH determinations.—Dr. Carmichael asserts that "experiments dealing with pH values assume as much significance as, if not more than, the microscopical experiments." I would point out that such experiments are not proof of a living virus. I emphasize this point because many critics have expressed the opinion to me that, if a change of reaction could be demonstrated, it would be proof of the existence of a living organism. The fallacy, in such an argument, is obvious, when one considers that a change in reaction can be brought about by enzymes or ferments, or indeed many chemical reactions. Hence, I cannot agree with the view that such experiments are of more value than microscopical observations.

The obvious fallacy in Dr. Carmichael's pH work is that he is attempting to measure the reaction of cultures, without knowing whether they are cultures or not. In other words, he is working without knowledge as to whether the factor supposed to alter the pH is present or not. It is obviously only by examining a culture under the microscope that one can know whether it is positive or negative, and therefore likely or otherwise to induce the change of pH.

Methods employed: Colorimetric.—As regards the colorimetric method employed by Dr. Carmichael, this was not employed in our Westminster work for the following reasons:—(*a*) The solution under investigation is already coloured; (*b*) it may be opalescent, and the precise degree of opalescence cannot be simulated in controls; (*c*) as Dr. Carmichael admits, a difference of 0·2 pH may be entirely missed by a colorimetric method.

Hydrogen electrode.—Dr. Carmichael did not use the method employed at Westminster Hospital. He states that this is impracticable for two reasons: (1) On account of the excessive frothing that occurs on bubbling the hydrogen through the albuminous fluid, thus allowing the platinum point to lie above the level of the fluid being tested and to become dry. Two comments may be made on this: (*a*) If excessive frothing occurred on bubbling the hydrogen, as he states, the technique was faulty. Either too much hydrogen was used (requisite amount = 2 bubbles per second), or the vessel in which the experiment was being performed was unsuitable. The methods of preventing this difficulty are so simple as to need no discussion; (*b*) naturally if one is so careless as to allow the platinum point to lie above the level of the fluid being tested, and to become dry, no result could be expected. Obviously no electrical circuit is in existence under such circumstances; (2) Dr. Carmichael states that if hydrogen is bubbled through a biological fluid, any easily dissociated carbon dioxide is removed from the mixture. He goes on to say that for this reason he discarded the method. This is the precise reason I adopted this method.

The purpose of carrying out pH experiments was to determine whether or not a specific change in reaction occurred in positive cultures. It is well recognized in dealing with such mixtures as broth and serum and cerebrospinal fluid, that a change of pH is bound to occur spontaneously, owing to the loss of carbon dioxide, in consequence of which it becomes more alkaline. In other words, one has to contend with a factor already present in control and disseminated cases, inducing a change of hydrogen-ion concentration. Therefore it seemed obvious that the best method one could employ was that in which this additional factor, spontaneously changing the reaction, was removed. Hence the hydrogen (Rideal) electrode described was employed, for in this, as Dr. Carmichael points out, "the process of bubbling removes any easily dissociated carbon dioxide from the mixture." This being the case, the variable factor involved by loss of carbon dioxide is removed from the experiments and one is left only with the factor which one is out to measure, namely, any variation in hydrogen-ion concentration induced by something specific to the cultures themselves. In addition, the essential point which I attempted to prove or disprove was whether any definite change as regards reaction was manifest in cultures from day to day. Obviously, it was important to

begin from precisely the same point each day, and therefore it was essential to remove this varying factor due to loss of carbon dioxide. Only in this way can one start from the same point each day, and compare results inherent to, and induced by, cultures themselves.

Many observers have investigated the hydrogen-ion concentration of both cerebrospinal fluid and serum, and have drawn attention to the fact, easily demonstrable, that both these fluids become alkaline after withdrawal. As regards cerebrospinal fluid, I carried out a series of observations in this respect in 1926. These were published in the *Quarterly Journal of Medicine*, 1927, vol. xxi. I quote from this paper: "During the first two hours after withdrawal the pH of cerebrospinal fluid rapidly increases from 7·3 to 7·9 or 8. In the next 12 hours the change is more gradual, and after 12 hours the pH remains practically constant, the final value 24 hours after withdrawal being about 8·1-8·5. The pH of fluid kept in an ordinary sterile tube with a cotton-wool plug, was compared with that of the same fluid collected beneath a layer of paraffin and kept tightly corked. After 2-8 hours, it was found that the pH of the latter fluid had retained its original value, or had even fallen, while the pH of the fluid in the tube with the cotton-wool plug only had become more alkaline, the pH changing from 7·3 to 8·1." I pointed out the obvious fact that "just as loss of carbon dioxide affects the reaction of the blood, so, unless the cerebrospinal fluid is collected and examined without loss of carbon dioxide, the reaction would appear more alkaline than it really is in the body." When, however, it comes to a question of making cultures of the cerebrospinal fluid, with a view to culturing a virus under aerobic conditions, it is obviously not possible to prevent this loss of carbon dioxide by collection under paraffin. A little consideration will show that the prevention of loss of carbon dioxide by this method will, at the same time, defeat the object of making the cultures, since the conditions of growth are not fulfilled. Therefore, the only alternative is to use a method for measurement of drogen-ion concentration in which this disturbing factor is eliminated.

Dr. Carmichael points out that when he incubates a mixture of broth, serum, and cerebrospinal fluid, the pH of the mixture rises to the alkaline side, reaching a level of 8·0 or more. It is difficult to see why he should expect it to be anything else, using the method he describes. The shift to the alkaline side would be inevitable by this method. He states that he carried out experiments to ascertain the cause of this shift of the pH to the alkaline side, and comes to the conclusion that it is due to the loss of carbon dioxide. In the initial stages of the work at Westminster Hospital this problem of loss of carbon dioxide, occurring in any mixture of broth and serum, and rendering the mixture more alkaline, as pointed out by many previous workers, was taken into consideration, with the result that this method was employed.

Dr. Carmichael states that if the lost carbon dioxide is replaced by placing the mixture in a partial pressure of carbon dioxide, equal to that of the alveolar air (6%), the pH values move to the acid side, only to return to the alkaline side after exposure to the ordinary atmosphere. Thus he provides confirmatory evidence of the well-recognized fact that alteration of the pH to the alkaline side is due to a loss of carbon dioxide. He goes on to say that "unless care is taken to avoid this loss, it is impossible to prevent the alteration of the pH of the mixture to the alkaline side after the addition of the cerebrospinal fluid," and he continues: "As such precautions were not adopted by the workers at the Westminster Hospital it is impossible to explain or repeat the figures they obtained for controls or for cultures of cerebrospinal fluid, using aerobic methods of cultivation." It would be interesting to learn how such precautions could be adopted, compatible with the obtaining of positive cultures. Collection under paraffin is obviously out of the question, since the cultures must be aerobic. The only alternative appears to be the adoption of a method whereby this loosely-held carbon dioxide was eliminated, hence the Rideal electrode was employed.

Dr. Carmichael states that the pH value of serum varies after filtration. In the work carried out at Westminster we have not found this variation to exceed 0·2 pH, but the same type of filter was employed, and not different ones as in his table. The average pH of serum after filtration was 8·2-8·4.

In his Table III Dr. Carmichael gives the pH readings of serum broth and various mixtures. In nine out of twelve cases he obtains a mixture in which the pH does not exceed 7·6, which is the requisite condition laid down in my publication for the preparation of cultures. That there is some varying factor, presumably due to loss of carbon dioxide, occurring in his experiments, is shown by comparing the four experiments quoted from his table. Thus:

	Serum	Broth	Proportions	Mixture
(1)	8·7	7·3	B. 10 c.c. C. 3 c.c.	7·5
(2)	8·4	7·3	B. 10 c.c. C. 3 c.c.	7·6
(3)	8·4	7·4	B. 10 c.c. S. 3 c.c.	7·9
(4)	8·6	7·4	B. 10 c.c. S. 3 c.c.	7·7

Thus, comparing (1) and (2)—using the same quantities of broth and serum—he uses in (1) serum as alkaline as 8·7, and gets a final pH of the mixture of 7·5; in (2) he uses a more acid serum, pH 8·4, and yet gets a more alkaline mixture of 7·6—the pH of the Hartley's broth being the same in both cases. Similarly, in (4), he uses a serum of pH 8·6, and gets a resulting pH of 7·7. While in (3) he uses a more acid serum and yet gets a more alkaline (7·9) mixture, the pH of the Hartley's broth remaining the same in both. The inference is that the method he is using is not suitable when dealing with mixtures in which the carbon dioxide content is constantly varying.

In my publication I repeatedly emphasized that it is essential to culture the cerebrospinal fluid immediately after withdrawal. Whether hydrogen-ion concentration is the most important reason for this, I am not at the moment prepared to say, but in all cases in which positive cultures have been obtained the pH of the cerebrospinal fluid when cultured was not greater than 7·4. In other words, the cultures consisted of a mixture of Hartley's broth, pH about 7·4, serum pH about 8·2 or 8·4, and cerebrospinal fluid pH 7·4, the resulting pH of the mixture being 7·5 to 7·6. It has been suggested by critics that if one employs the hydrogen electrode method, in which hydrogen is bubbled through the mixture, the initial pH of the mixture would be the same whether the cerebrospinal fluid was added when fresh, or after standing, because in either case the carbon dioxide would escape from the cerebrospinal fluid and render it more alkaline. On the contrary, the reverse is the case. Hartley's broth is a well-buffered medium, and, in fact, was originally employed in the production of diphtheria toxin, in order that reasonable amounts of acid or alkali should not appreciably affect the reaction. The comprehension of the pH experiments in this work depends essentially upon the recognition of this buffering capacity of Hartley's broth. In the first place, as regards cerebrospinal fluid, if this is added when the pH is 7·4, owing to this buffering action the carbon dioxide is converted into bicarbonate. In consequence of this, when the Rideal electrode is used, the carbon dioxide is no longer removed, as it would be in the case of cerebrospinal fluid alone, and a pH of 7·5 to 7·6 results. On the other hand, if cerebrospinal fluid is added to a mixture of broth and serum at a time when loss of carbon dioxide has occurred, and the fluid is therefore alkaline, the correct pH cannot be attained.

Experiments carried out in my laboratory demonstrate this point. In these, carbon dioxide was actually bubbled into Hartley's broth, of known pH for varying periods of time, and subsequently hydrogen was bubbled through as in ordinary pH determinations. It was found that the pH fell from 7·5 to 6·9 or 6·8 (average of experiments) on bubbling carbon dioxide through the broth for about 20 minutes. Subsequently, when hydrogen was blown through and a reading taken at intervals of 10 minutes for four hours, the galvanometer remained practically constant, approximately the same pH being maintained, demonstrating the points I have endeavoured to emphasize as regards Hartley's broth and carbon dioxide.

Supposing one takes a mixture of Hartley's broth, serum, and cerebrospinal fluid (normal), in the proportions of 12 c.c. of Hartley's broth, pH 7·3, 3 c.c. of serum, pH 8·2, and cerebrospinal fluid 5 c.c. pH 7·4. If now the pH is determined, using a Rideal electrode, it will be found to be about 7·5 or 7·6. During incubation there is loss of carbon dioxide. In consequence, if the pH is taken again after 24 hours, it will take slightly less time for the galvanometer to give a steady reading, since there is less loosely held carbon dioxide remaining to be blown off by the hydrogen. Obviously, the reading would come about the same as the first reading, for in both cases the varying factor of the loosely held carbon dioxide has been removed and there is no other factor inducing any change of reaction. But it will be clear that this similarity of readings can only be obtained if this particular method is used, in which the variable factor of the loosely held carbon dioxide is removed. By any other method in which this is not removed, the readings will not be similar, but the second will be more alkaline than the first, because carbon dioxide has been lost, during incubation. This is the case using cerebrospinal fluid from control cases, normal and pathological. On

the other hand, if some change has occurred through growth, then the first and second readings, after removal of the carbon dioxide, would not be the same. As regards disseminated sclerosis cultures, it must be emphasized that this change of reaction, presumably due to some inherent property of the cultures themselves, is of very small magnitude, i.e., in the neighbourhood of not more than 0·1, or at the most 0·2 pH variation daily. Hence it is easily conceivable that it might be masked by the more pronounced alkaline shift of pH due to loss of carbon dioxide.

It will be readily understood that the degree of buffering action of the Hartley's broth depends, to a certain extent, upon the amount used. In my publication, apart from the table showing the results of a few illustrative experiments, I find that I do not mention the amount of Hartley's broth, serum, and cerebrospinal fluid which should be mixed for cultural work. The point emphasized, however, is that the initial pH of the culture must be 7·5 or 7·6, and this really means that the mixture of Hartley's broth and serum must be of a pH of 7·5. The precise amount of Hartley's broth which must be added to produce this pH depends, of course, on the initial reaction of the Hartley's broth when made, and as this varies slightly in different batches of media, figures illustrative of the amount to be added were not mentioned. In addition, there is the variable factor of the pH of serum to be taken into account. Thus, in the case quoted in my paper, where 10 c.c. of Hartley's broth, 3 c.c. of serum, and 8 c.c. of cerebrospinal fluid were used, the pH of the Hartley's broth was about 7·1. If the pH of the Hartley's broth is 7·4 to 7·5 it is usually necessary to add about 12 c.c. of Hartley's broth, if the pH of the serum is 8·2 to 8·4. It was specifically pointed out in my publication, that the change of reaction only occurs in actively growing cultures. I quote my precise words: "It occurs only in *actively growing cultures*, but the exact mechanism of the change remains a problem for future investigation." Therefore, it is surely reasonable, in repeating the work, to examine the culture microscopically *first* and be sure that one *is* dealing with an actively growing culture, before attempting to determine the pH of the mixture. Otherwise it is not known whether the conditions requisite for inducing this change of reaction are fulfilled.

It might be argued that in my very early work on this subject four years ago a change of reaction was the first thing noticed. I would like to point out that a very large number of cultures were made from disseminated fluids, and as I say in my publication: "Numerous unsuccessful experiments carried out." In these early experiments negative results were so uniform as to be completely discouraging, and only in a few isolated cases out of this large number examined was any change of reaction manifest." I emphasized this point in my publication unduly perhaps, but because it was the starting point of the investigations subsequently carried out. Uniform results were not obtained until later in the work when the somewhat difficult technique was rendered much more perfect and the scientific basis, namely the microscopical appearance of cultures, established for the pH experiments. Even in this early work I held the opinion that this occasional change of reaction demonstrable was valueless, unless it could be correlated with either a microscopical appearance or some other property inherent to the cultures.

The microscopic appearance of cultures.—Dr. Carmichael examined nineteen cultures of disseminated sclerosis. Of these eleven presumably fulfilled the condition laid down in my paper, namely, that the fluid must be cultured immediately after withdrawal. I quote from my paper:

> "Transference of the material, either before culturing or before microscopical examination of the cultures, is very undesirable. Such a procedure leads to unreliable and inconstant results, although the reason for this is not, at the moment, perfectly clear."

Presumably the cultures made at Queen Square fulfilled this condition and were negative. I would point out that anyone who attempts to compare this work with ordinary bacteriological observations, and expects uniformly positive results, is in ignorance of the fundamental principles involved. The extreme difficulties of the technique are enhanced by the fact that one can never see any visible growth except by the somewhat elaborate microscopical examination involved. When, in my publication, I speak of a certain percentage of positive results I should perhaps emphasize that many of these represent more than one examination of the fluid of that particular patient. In the work published analogous experiments were carried out in controls in which the fluid was examined from patients who came periodically to hospital for anti-syphilitic treatment.

Dr. Carmichael states that Mr. Barnard examined eight cultures which he prepared, and in them found nothing distinctive. I understand by this that Mr. Barnard did not see, in these cultures, the appearance of spheres and granules which he saw in my cultures at Westminster.

The criticism most commonly met with, and the error into which most workers have fallen, is the confusion of spheres seen in uninoculated media with those characteristic of cultures made from cerebrospinal fluid from cases of disseminated sclerosis. The fact that spheres do appear in uninoculated tubes, using the optical system described, is undoubtedly one of the chief difficulties in this work, which should only be undertaken after careful and prolonged observations, and thorough cognizance of the various artefacts and contaminants which may be met with. I quote the words of Mr. Barnard, dealing with this question in my publication:—

> "It is admitted that bodies do appear on occasions in uninoculated tubes that have some points in common with both pleuro-pneumonia and the organism observed in disseminated sclerosis cultures. There is reason to regard these as filterable contaminants, but they can be microscopically differentiated from the cultures herein described, and further, they develop best at different temperatures and in different times. By analogy, therefore, there is reason to regard the results obtained in culture as being suggestive of the growth of a living virus, although much has yet to be done before a full and satisfactory understanding of the complete life-cycle can be worked out."

As Dr. Carmichael mentions in his paper, I was supplied with 32 specimens of cerebrospinal fluid from various sources; of these 14 were contaminated and therefore unsuitable for cultural purposes, and no spheres or colonies were seen in any of the cultures made from any of these fluids, though I understand that one was reported positive through a secretarial error.

Dr. PHYLLIS M. T. KERRIDGE, speaking with regard to the technique of the measurements of the hydrogen-ion concentrations, said: Anyone who has used the hydrogen electrode will have sympathy with those working with this electrode in solutions containing protein and carbon dioxide. On general theoretical grounds one would have said that the Bailey type of electrode used by Dr. Carmichael was the better for the purpose, and that the results which he obtained were those which would be expected. Nevertheless it seems inevitable that more carbon dioxide must have been lost in the experiments of Miss Chevassut, using the Rideal electrode, and it appears to me to be significant that in spite of this she observed a large acid change. Her controls seem to be adequate. The work of Dr. Carmichael does not offer any explanation of the acid change observed by Miss Chevassut.

Dr. JOHN MARRACK said it would be impossible to remove all the free carbon dioxide from fluids of the pH under discussion within reasonable time by bubbling hydrogen through at two bubbles a second. At pH 7·5 for example about one twenty-fifth of the carbon dioxide would be free, and as long as the pH remained about that value this proportion of free carbon dioxide would be maintained by the splitting off of combined carbon dioxide. Thus all the carbon dioxide present would have to be removed before the free carbon dioxide was removed. The pH found would be intermediate between the actual pH of the fluid and that which would be obtained by complete removal of carbon dioxide, and would have no constant relation to either.

Section of Ophthalmology.

[*December* 12, 1930, *continued.*]

Two Cases of Exudative Choroiditis in Children.—J. COLE MARSHALL, F.R.C.S.

These are two somewhat exceptional cases of the condition occurring in children.

(1) E.D.M., a boy, aged 8. In the right eye there is a fluffy mass hanging over the right superior temporal vein, and also a marked white protuberance just outside the macula region (fig. 1); the vision in this eye is $\frac{6}{24}$ and in the left eye it is $\frac{6}{6}$.

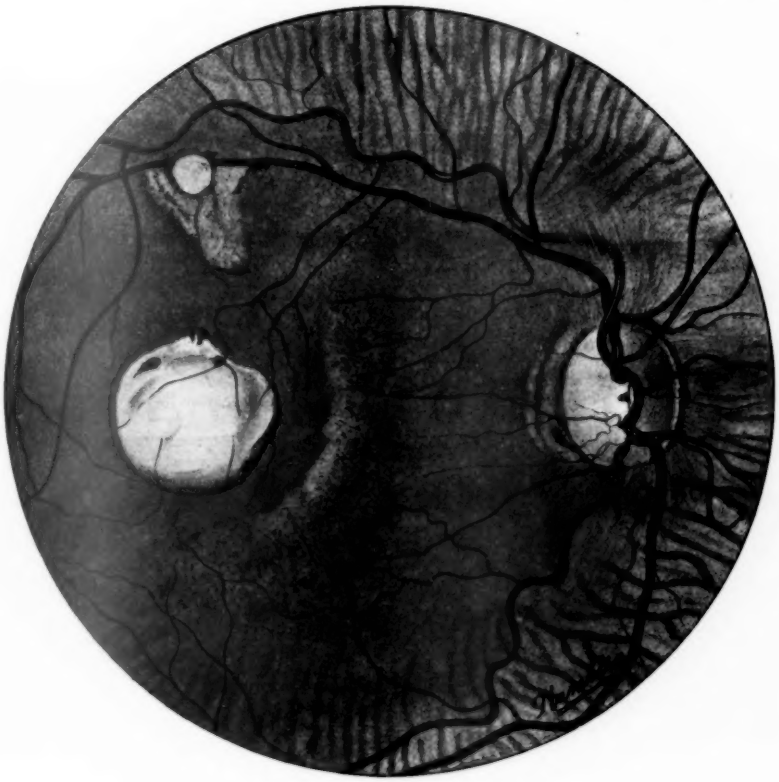


FIG. 1.—E. D. M. Right Eye.

(2) E. D., a girl, aged 9. In the right eye there are large patches of choroidal atrophy round the disc extending nearly to the macula, also large patches of atrophy in the upper and outer part of the periphery (fig. 2). The vision in this eye (right) is $\frac{6}{24}$.

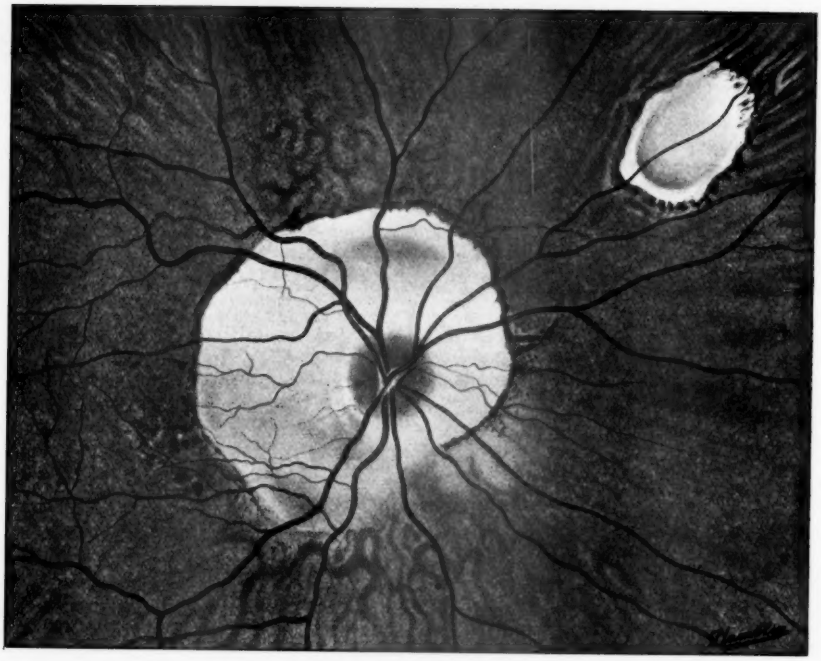


FIG. 2.—E. D. Right Eye.

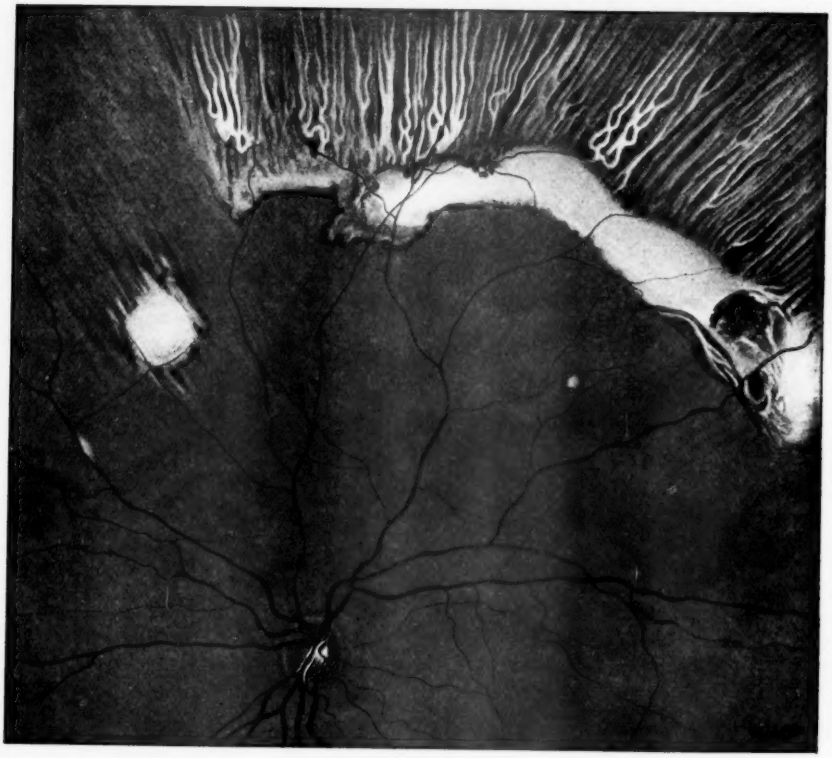
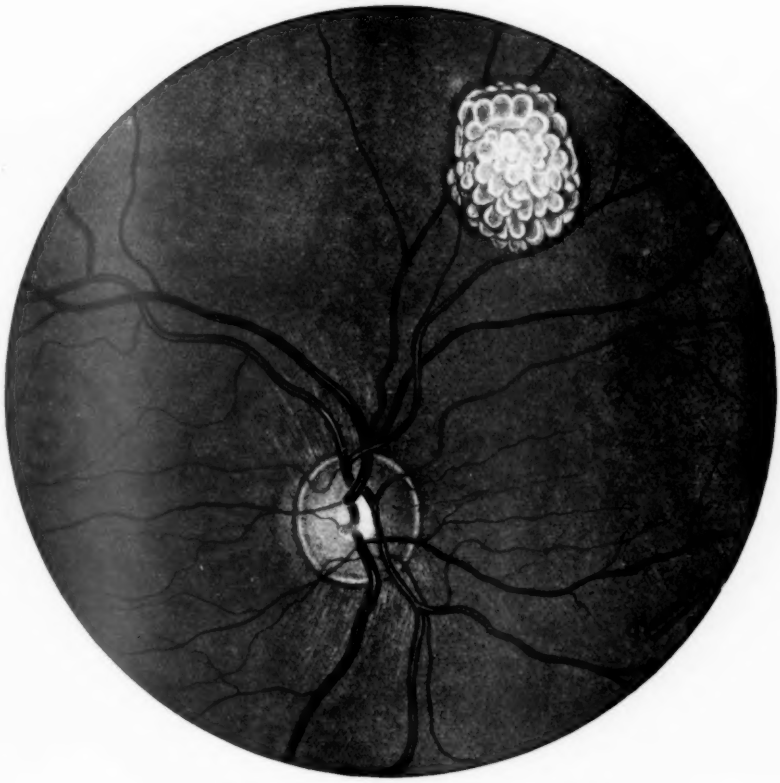


FIG. 3.—E D. Left Eye.

In the left eye there is a very large patch of atrophy, concentrically placed near the periphery, and small patches scattered over the fundus, upwards and inwards (fig. 3). The vision in this eye is $\frac{6}{6}$.

Abnormality of Fundus: Case for Diagnosis.—D. V. GIRI.

F. J. D., male, aged 28, first seen by me October 16, 1930, at the Royal Eye Hospital, Eastbourne.



A rare solitary formation in an otherwise healthy fundus.

History.—While he was rowing on the river about six months previously a small bud from an overhanging branch caught him in the left eye. A piece of this was removed by his doctor but he thinks there is still something there. Eyes water after reading.

The patient is under treatment for syphilis at the V.D. Clinic.

Examination.—Right vision with − 2 sph.+ 4 cyl. axis 75° upwards and inwards $\frac{6}{6}$ nearly. Left vision with − 2 sph.+ 3·25 cyl. axis 120° upwards and inwards $\frac{6}{6}$ nearly. Pupils active. Both eyes: tension normal digitally. Left eye: media clear, fundus normal. Right eye: media clear. The fundus shows a dead white prominence looking like a truncated strawberry, a pine cone, or the flower popularly known as "snowball" (see fig.). It is about 2 P.D. (papilla diameter) across and, situated about 2 P.D. upwards and inwards from the papilla. The retinal vessel on the nasal side passes over the side of the eminence. It is best seen with the Gullstrand ophthalmoscope, binocularly. Apart from this, the fundus is normal. Ophthalmoscopy in red free light reveals nothing special.

This is the first time that such a fundus abnormality has come under my observation. What is the nature of the formation? Is it dangerous? What intervention, if any, does it call for?

I have referred to Oeller's "Atlas of Ophthalmoscopy," which is considered the most exhaustive, "Adam's Ophthalmoscopische Diagnostik" (Urban and Schwarzenberg, 1912), and Dimmer's "Der Augenspiegel" (Franz Deuticke, 1921). In none of these is there a picture corresponding to my case.

Discussion.—Mr. R. AFFLECK GREEVES said he regarded this as a typical colloid body formation on the surface of the hyaline membrane of Bruch. It was similar to those one saw on the edge of the optic disc, where they were of more common occurrence. These outgrowths were formed behind the retina, and when they were very large the overlying retina became atrophied. He thought these bodies of large size were congenital in origin, and were usually discovered by chance. They did not affect vision, and he did not think they became larger.

Mr. M. S. MAYOU said he thought that this was a case of hyaline nodule in the retina. These nodules were often described as looking like bunches of grapes, and were principally found in retinitis pigmentosa, and then they were nearer the disc. He had sections from such cases in which the hyaline change was away from the optic disc, especially in eyes with congenital malformations and undergoing degeneration.

Author's Postscript.—Most of the Members present at the meeting saw the case. Mr. Bernard Cridland said he had seen something similar, and I believe Mr. Doggart said that he had had a similar case under observation at St. Thomas's Hospital for over a year, which had not yet been diagnosed and which had remained unchanged.

My impression is that it looks like a smooth structure with translucent cells and opaque walls. As the Gullstrand binocular ophthalmoscope was not available at the meeting the Members could not get such a good view of it as I have had. Owing to the difficulty of representing a complicated rounded structure on the flat, the picture reproduced is only an approximation. I am not aware of any anatomical finding to show that excrescences of the lamina vitrea—colloid bodies—form such a prominence; moreover, they are not so white and dull, have generally some pigment round them, and are usually found in the eyes of elderly individuals, hardly ever singly.

I have discussed drusen in detail in my paper "On Concretions in the Optic Nerve" (*The Ophthalmoscope*, 1913, xi, 390). The consensus of opinion is that they are of hyaline constitution. Parsons considers it probable that hyaline deposits are really albuminous exudates undergoing gradual chemical change ("Pathology of the Eye," vol. ii: Hyaline bodies [drusen]). They are mostly found in eyes gravely diseased or atrophic from injury. They appear somewhat like a number of tiny glistening translucent beads put together side by side and almost invariably occur either in the neighbourhood of the central retinal vessels or at the edge of the disc. Dimmer thinks they arise only from the optic nerve-head.

In the present case the patient is young. There is no history or sign of injury

to the right eye; it is healthy with a perfectly normal fundus but for the solitary peculiar formation, which, as shown above, hardly fits in with either colloid bodies or drusen. Hence my diffidence to call it by either name.

Spasmodic Entropion treated by Injection of Alcohol.—ARNOLD SORSBY, F.R.C.S.

G.C., male, aged 69.

History.—Right eye lost through perforating corneal ulcer, eleven years ago.

Treatment.—Injection of 20 minims of 4% novocain, followed five minutes afterwards by an injection of 20 minims of 80% alcohol. Results satisfactory. No relapse after two months.

(Case shown by courtesy of Mr. T. W. LETCHWORTH).

References.—SAFAR, K., *Zeitschr. f. Augenheilk.*, 1930, lxxi, 135. WEEKERS, L., *Arch. d'Ophtal.*, 1928, xlv, 20.

Glaucoma associated with Facial Nævus.—ARNOLD SORSBY, F.R.C.S.

A. P., male, aged 34.

History.—Right eye said to have been blind since infancy. First available notes date back to 1918. Right eye then had no perception of light; tension + 3. Lens opaque, and the present external condition was observed.

Vision.—Right: no perception of light; tension + 3. Left: $\frac{6}{9}$, tension normal. Nævus of sclerotic and conjunctiva of right eye very large, involving practically whole of right half of face; thickening of all the tissues including right half of lips and buccal mucosa. No buphthalmos. Left eye, normal. The patient also has a large nævus on the midline of the back.

Diagnosis.—Probable nævus of choroid.

(Case shown by courtesy of Mr. A. D. GRIFFITH.)

References.—[1] BALLANTYNE, A. J., "Buphthalmos with Facial Nævus and Allied Conditions," *Brit. Journ. Ophthal.*, 1930, xiv, 481. [2] PATON, WILLIAMSON-NOBLE and GREENFIELD, "Capillary Angiomatosis" (Lindau)," *Trans. 13th Internat. Cong. of Ophthal.*, 1929, 624. [3] HUDELI, A., "Glaucome et Nævus facial," *Annal. d'Oculist.*, 1929, clxvi, 889. [4] KRAUSE, K., "Nævus flammeus und Glaukom," *Zeitschr. f. Augenheilk.*, 1929, lxviii, 244. [These four papers contain extensive bibliographies.] [5] DEHOGUES, J. L., "Glaucome et Nævus facial," *Annal. d'Oculist.*, 1930, clxvii, 580.

Two Cases of Latent Nystagmus.—ARNOLD SORSBY, F.R.C.S.

(I) D. L., male, aged 11.

History.—Left convergent squint since age of two years. No nystagmus with both eyes open. Nystagmus on covering one eye.

Vision.—Right = $\frac{6}{24}$; left = $\frac{6}{60}$. Both eyes together = $\frac{6}{12} - \frac{6}{9}$.

(Case shown by courtesy of Mr. A. H. LEVY.)

(II) K. H., female, aged 14.

History.—Old case of ophthalmia neonatorum. High myopia, slight or no nystagmus with both eyes open. Marked nystagmus on covering one eye. Vision with each eye separately = $\frac{6}{60}$. Both eyes together = $\frac{6}{24}$.

(Case shown by courtesy of Mr. T. W. LETCHWORTH).

Reference.—SORSBY, A., "Latent Nystagmus," *Brit. Journ. of Ophthal.*, 1931, xv, 1.

Discussion.—The PRESIDENT said there was binocular perception present, that is to say, the first stage of binocular vision. In many cases this was enough to control the nystagmus to a considerable extent. If both external recti were advanced, besides curing the squint in the first case, the tightening of the muscles would reduce the nystagmus still further.

Mr. SORSBY said that two cases of latent nystagmus, in which an eye had been lost, had been reported. In one case the nystagmus became permanent, in the other it was only periodic. That the marked decline in vision obtained on covering one eye was due to the nystagmus could be seen from the fact that vision increased at once when the nystagmic eye was fixed with forceps.

Section of Anæsthetics.

[*February* 6, 1931.]

Spinal Analgesia with Special Reference to Operations above the Diaphragm.

By A. Dickson Wright, M.S.

If we take a general view of all methods of anæsthesia, we can say that there are two distinct kinds of method whereby operation and childbirth can be rendered painless.

(1) Those in which the blood is charged with a drug which in passing through the central nervous system produces a condition of temporary coma during which the patient is unaware of the painful stimuli that still reach the central nervous system. At the same time all motor stimuli cease to emanate from the brain except those necessary to maintain respiratory and circulatory function. The drug is introduced into the circulation by every conceivable route: by the lungs—by normal respiration or tracheal catheter—by the stomach, by the veins, by the subcutaneous tissues, and even by the rectum and colon.

(2) Those in which the nerves are attacked and the central nervous system, instead of being perfused with a narcotic, is temporarily isolated from painful stimuli by the blocking of the nerves with a drug, generally of the cocaine group. The nerves may be attacked in any part of their course from the spinal cord to their destination.

In their extrathecal courses, the injection of nerves is difficult and uncertain, but their injection in the subarachnoid space is both simple and certain. All the nerves in the body, without exception, traverse this space, so that for a short part of its course every nerve in the body is surrounded by cerebrospinal fluid. My personal view is that in this fluid space lies the future of anæsthesia.

It must at the outset be clearly understood that "spinal" anæsthesia belongs to this second group. There are many misconceptions on this point, arising from the caption "spinal," which leaves the impression that the anæsthetic acts upon the spinal medulla, and, if high enough, on the medulla oblongata. It is certain that nothing of the kind occurs; the injected anæsthetic acts upon the nerve roots only, and the true title for this form of anæsthesia is "selective intrathecal nerve block." The reason for the prefix "selective" will now be considered.

If a mixed nerve of the body is bathed with a weak solution of a member of the cocaine group, it is found that the conductivity of the nerve is not abolished in all respects immediately, but the power to convey the different types of stimuli disappear in a certain order. I have found that the following order is followed: (1) The epicritic fibres are blocked so that the patient, while conscious of deep pressure, is unaware of pain in the area blocked. (2) The fibres of temperature sensation are interrupted. I have noticed in practice that sometimes an operation under nerve block can be carried out with the knife when the diathermy needle causes pain. (3) The sympathetic fibres are interrupted. Use is made of this in injections of the sciatic nerve for trophic or ischæmic ulcerations of the feet, and more recently in White's most ingenious test for the differentiation of spastic from organic arterial defects of the extremities. (4) The motor fibres and fibres conveying deep sensation go last of all.

Thus we see that local anæsthetics have a selective action on an isolated mixed nerve; but in addition to this there are certain anatomical factors which prevail in the subarachnoid space which makes the anæsthetic administered in the theca still more selective:—

(1) The subdivision of the theca into imperfect anterior and posterior compartments by the spinal cord, ligamentum denticulatum, and the nerve roots themselves.

(2) In the posterior compartment lie all the sensory roots of the spinal nerves, and therefore these receive the full effect of an injection made into the posterior compartment.

(3) The sensory root expands into a flat brush before entering the cord, and so exposes the maximum area to the anæsthetic and quickly adsorbs and fixes a great part of it before it reaches the anterior roots. It will be remembered also, that the anterior roots are more compact, as they are not spread out so as to enter the cord along a definite straight line, as in the case of the posterior roots. The difference between the two roots is that of the two usual types of paint brushes, the posterior of the flat type, and the anterior of the pencil type. It is probable that because of this arrangement the posterior roots have a greater absorptive capacity.

(4) I have formed the impression that the motor nerves are of a firmer consistency than the sensory. Especially in the case of the trigeminal has this been observed. This may also diminish the absorptive capacity of the motor roots.

(5) Some of the roots are much bulkier than others, as in those of the cervical and lumbar enlargements, so that there is often incomplete paralysis of the limbs, while full abdominal relaxation is obtained.

It is thus seen that the term "selective" in connection with intrathecal nerve block is justified on two grounds. Firstly, because of the selective action of the anæsthetic on the nerve constituents; secondly, because of the anatomical dispositions of the nerve roots in the theca.

The historical side of spinal anæsthesia is of some interest. It was no less than 45 years ago that Corning of New York first suggested and practised the method of using cocaine. Bier in Germany in 1898, and Tuffier in France in 1900, reported their experiences with operations, chiefly below the umbilicus, using intrathecal cocaine in small doses.

It was quickly noticed that the anæsthesia produced by intrathecal cocaine was by no means confined to the lower parts of the body. After a varying interval of time after the injection, it was observed that the anæsthesia crept up over the chest, up the arms, over the top of the head, and finally the face was anæsthetized, so that on many occasions a general anæsthesia was produced when the operation was only for the legs. Payne, following Morton, made practical use of this discovery in America, and in 1902 reported seven operations on the mastoid, middle ear, frontal sinuses and eye performed with intrathecal cocaine anæsthesia. Remarkable to say, one of these operations was performed with the patient sitting in a chair.

Since these early days of spinal anæsthesia, various surgeons have taken up the method, in some cases almost to the total exclusion of other types of anæsthesia. For instance, Koster and Wells in America, Delmas and Le Filliatre in France. Le Filliatre found it particularly valuable in the war in extensive multiple wounds, as two or three surgeons could work unhampered on the same patient at the same time.

The drugs used have changed with the passage of time and, with one exception, have all been of the cocaine group. In 1895 tropacocaine was introduced, in 1904 stovaine was discovered by Fourneau, and Einhorn produced novocain. The tendency in each case was to reduce the toxicity of the drug, but as a set-off to this it was found that toxicity and anæsthetizing powers seemed to be in direct ratio and as the toxicity was reduced, so the effective dose had to be increased. There also seemed to be some diminution in the selective faculty of the drug as a result of the reduction of the toxicity; of all these modifications none equals cocaine in this respect. For this reason there has been a tendency on the part of certain surgeons to revert to cocaine. It is said to be possible with this drug to produce a total anæsthesia of the body without any paralysis at all, and this can be said of none of the others.

"Anhydrous cocaine" is the peculiar title given by Wells to cocaine purified by precipitation from alcoholic solution by ether. The crystals so precipitated are used without further sterilization and are stated to be freed by this process from a highly toxic substance formed by the deterioration or heat sterilization of cocaine.

The recent addition to local anæsthetics—percain—is a new departure, as it is in no way connected chemically with cocaine but is allied to another local anæsthetic viz., quinine. It has a toxicity even greater than that of cocaine, but it is a wonderfully powerful local anæsthetic and gives an anæsthesia of greater duration.

It might be mentioned here that novocain has a proper chemical name, viz., "ethocaine," and for the bewilderment of surgeons and the satisfaction of the manufacturing chemists, masquerades under the following names: neocain, planocain, procain, kerocain, holocain, durocain, spinocain and novutox.

The drug in solution is introduced to the subarachnoid space as a rule, by a fine needle through one of the lumbar spaces. The sacral hiatus has been used intentionally as a route for administering intrathecal anæsthesia. Occasionally it has been unwittingly used while administering caudal block, sometimes with fatal results. Dorsal and even cervical injections have been used, and I have on two occasions myself given the anæsthetic by cisternal puncture. The drug is dissolved in saline, distilled water, or the cerebrospinal fluid itself, and given in varying strengths. Sometimes a concentrated solution is diluted with cerebrospinal fluid before injection. By some a little air is injected with the fluid to keep away headaches, and by others various stimulants such as adrenalin, caffein and strychnine are injected mixed with the anæsthetic solution. Inert substances are sometimes added to alter specific gravity or delay absorption; such are mannitol, starch and magnesium sulphate.

It must be borne in mind that however or wherever injected, the solution only acts on the nerves. The brain and cord substance is protected by its pial covering, and the phrenic nerves—but only up to a certain point—are protected by the selective action of the drug.

The production of total anæsthesia of the body by intrathecal injection can be made certain in a number of ways:—

(1) By increasing the dose of the drug. Doses of over 500 mg., or 8 gr., of novocain will almost invariably produce total anæsthesia, no matter what the strength or specific gravity of the solution used or the point of injection or the position of the patient after injection. The largest dose injected is recorded by Goetz, who injected no less than 1,200 mg., or 18 gr., without harm resulting.

(2) By increasing the volume of the solution injected. Thus 25 c.c. of 1% novocain will produce a total anæsthesia and, strange to say, it is not necessary to withdraw cerebrospinal to make room for this volume of solution. There is a remarkable mechanism for disposing of excess fluid in the subarachnoid space and large quantities of fluid can be injected and absorbed without symptoms of increase of intracranial pressure.

(3) By withdrawing a quantity of cerebrospinal fluid and diluting the anæsthetic with this. Thus Koster, for total anæsthesia, dissolves 300 mg. novocain in 8 c.c. of cerebrospinal fluid, and for less extensive anæsthesia reduces both drug and fluid. Delmas recommends the withdrawal of 50 c.c. of fluid and reinjection with the anæsthetic.

(4) By "barbotage," as first recommended by Le Filliatre. This consists of injecting part of the anæsthetic solution and then withdrawing cerebrospinal fluid and repeating this process several times. There is thus a churning up of the cerebrospinal fluid and the anæsthetic is distributed far and wide.

(5) By increasing the force of the injection. This undoubtedly has great effect.

(6) By altering the direction of the injection in an upward direction (Wells).

(7) By making the injection at a higher level. Jonnesco first recommended this and described the production of zones of anæsthesia by injection of small quantities of anæsthetic at the level required for the operation.

(8) By using cocaine, whereby total anæsthesia can be gained even with minimal doses, it being necessary only to use larger doses to secure greater duration of anæsthesia.

(9) By using a solution of a different specific gravity from the cerebrospinal fluid and distributing the fluid after injection by placing the patient in a suitable position. Sometimes the solution is made less diffusible by adding a viscous substance to it, such as starch, so that it will obey the laws of gravity rather than those of diffusion. The addition of these substances seems to create a disproportionate increase in the cost of the anæsthesia. I have been unable to satisfy myself that this method of securing general anæsthesia is of much value compared with the previous eight methods. In a very effective injection it sometimes happens that the central nervous system is so effectively cut off that the patient goes to sleep or even becomes unconscious for a time.

The disadvantages of spinal anæsthesia make a formidable list, but there are methods of overcoming most of them and, moreover, many of them are of such great rarity as to be of little importance. I will try to give them in their order of importance :—

(A) *During anæsthesia :* (1) Death is associated with all anæsthetics, even with nitrous oxide and resuscitants like carbon dioxide. But we are all most anxious to avoid the death on the table because it is so tragic and because of the inquiry that follows it. A patient may aspirate his vomit through being left unattended and die a month later from an abscess in his lung, but the anæsthetist will not suffer the inconvenience and loss of reputation which follows an operative death from unforeseen and unforeseeable coronary atheroma. I have had one death on the table in a boy who had little hope of life as he was suffering from a terminal infection of ascites. In Koster's series of 6,000 cases, only six deaths occurred and of these only two could have been regarded as those of healthy individuals taken away in the prime of life, ; the remaining four were all desperately ill. Spinal anæsthesia has earned an evil reputation for sudden death because by many it is only used occasionally for those patients whom they regard as too ill for a general anæsthesia. Such patients are prone to die and such surgeons not to know the few essentials necessary to make the patient safe.

To prevent death the head-down position must be maintained till the anæsthesia has worn off, and intravenous or intracardiac adrenalin used for collapse or death as the case may be. In intravenous adrenalin one has such a wonderful restorative that I always feel that I have my patient safe when he is under a spinal anæsthetic. There is no such certain antidote in general anæsthesia.

(2) The nervous strain on the patient may be considerable but is a variable factor. This may be allayed, when necessary, by hypnotics like morphine and nembutal, but I am disinclined to multiply the drugs that a patient receives. It is no uncommon thing for as many as six separate drugs to be administered nowadays to secure anæsthesia.

(3) Fall in blood-pressure is dreaded by some and welcomed by others. It can be combated by intramuscular adrenalin or ephedrine, given as a preventive measure, or by intravenous adrenalin given after the fall has occurred. With experience one comes to ignore this fall as not dangerous and even as valuable for rendering operating clean and bloodless.

(4) Vomiting is a most annoying thing to patient and surgeon. It always seems worst when one is performing rough gastric or duodenal manipulations. It also seems to be associated with the fall in blood pressure. It can be kept down by pre-operative hypnotic inhalations of oxygen, and Labat likes to apply cold water and ice to the forehead and nape of the neck for this purpose. Most important of preventives is to abstain from intra-peritoneal manipulations till the patient is fully anæsthetized, and to abstain from rough handling in the vagus nerve area.

(5) Shallow and slow respiration may be worrying, and occasionally the patient feels that he cannot breathe and is upset because he cannot talk. The colour, however, remains excellent and there is little cause for worry. The slowest

respiration I have encountered is six per minute; the patient was asleep and I did not care to wake her up to tell her to breathe faster.

(6) Inadequate duration is a great disadvantage in long operations on the upper abdomen.

(*B*) *Post-operative.*—(1) Headache is a most variable complication and always greatly exaggerated by that opponent of innovations—the nursing sister. It is generally easily controlled. I have rarely had a case of the fierce headache for which lumbar puncture and intravenous hypertonics are necessary.

(2) Vomiting is much less than after other anæsthesias and is generally due to the type of operation rather than to the anæsthetic.

(3) Backache is of the type one would expect from muscular relaxation on a metal table for an hour, and occurs with other anæsthesia.

(4) Profound damage to nervous tissue producing paraplegia, hemiplegia, anterior poliomyelitis, etc., are almost unknown nowadays.

(5) Temporary or permanent paralysis of certain nerves, such as the pudic nerves and the abducens. This I have never encountered; it is said to be more common with stovaine anæsthesia. Temporary blindness of five days' duration has been reported in high spinal anæsthesia with cocaine.

(6) Meningitis is exceptionally rare; meningismus is occasionally encountered. I have had one case of diplococcal meningitis occurring twelve days after a spinal anæsthetic, given during a hospital epidemic of this disease.

(7) Psychic changes following operation are extremely uncommon (such as neurasthenia, sexual impotence, hypochondriacism, etc.).

The advantages of spinal anæsthesia are numerous.

(1) *It saves lives in certain conditions:* (*a*) In the case of a surgeon who is unable to obtain the assistance of good anæsthetists. The most dexterous surgeons have the most skilful anæsthetists who give abdominal relaxation to the patient and mental relaxation to the surgeon. The surgeon most in need of help gets the least. (*b*) In certain conditions, such as operations entailing much shock, or in intestinal obstruction, it is a real life saver. Some surgeons add spinal to general anæsthesia to prevent shock, but of all forms of combined anæsthesia, this is surely the most unnecessary and dangerous. The fall of blood-pressure with intrathecal anæsthesia is sometimes confused with shock, but this is due to ignorance of the true nature of the condition.

(2) *It is preferred by the patient in many cases*, and in none more than that of the patient writhing with the pain of a duodenal perforation. He never forgets the surgeon who stopped his pain in thirty seconds. I could multiply the number of low operations for which I prefer it, but time does not allow. For the high operations I prefer it to general anæsthesia in the following conditions:—

(i) Thoracotomy. Here it is an ideal anæsthetic, the quiet opening of the pleural cavity thus secured is a great advantage. I use it for all empyemata, operations on the lungs, œsophagus and pericardium. In thoracoplasty the reduction in bleeding is a satisfactory feature.

(ii) For dissections of the neck it is an excellent anæsthesia, minimizing the bleeding and giving good relaxation of the muscular structures. Ligation of the jugular vein does not seem to disturb the patient in any way.

(iii) For operations in the upper abdomen, cholecystectomy, gastrectomy, and above all, for splenectomy, it makes for easy operations.

(iv) For operations on the arm and hand, anæsthesia with preservation of vo untary movement of muscles is an obvious advantage in many cases.

(v) In operations on the thyroid, the reduction in bleeding is a welcome aid, as is the freedom from bloating of the tissues with local infiltration.

(vi) For operations on the mastoid region it is useful and may make for greater gentleness in an operation often roughly performed. The facial nerve seems to be a little safer with this form of anæsthesia.

(vii) For operations on the eyes. It is said to be very good for squint operations, as the patient coöperates in the correction of the deviation.

(viii) For craniotomies it is of value, provided that increased intracranial pressure does not preclude lumbar puncture.

In conclusion, spinal anæsthesia is a helpful anæsthesia to the surgeon who needs most help. It is a regular and uniform mode of anæsthesia; the technique is easily acquired, and above all, with a few precautions, it is safe and an antidote is always at hand. In certain conditions it is the means of saving many lives and in others of preventing much suffering. In cases of threatening gangrene it gives the diagnosis of the cause, and enables the surgeon to decide between sympathectomy and amputation.

The contra-indications are only three in number :—

(1) Increased subarachnoid pressure. (2) Septic conditions of the spinal column itself. (3) Perforations of the small and large intestines.

The extension of the method to the upper part of the body followed automatically when it was found that in about 30% of the cases having abdominal operations there was a total anæsthesia of the body, and when it was realized that the upper abdomen has a cranial and cervical sensory nerve supply. Many different and certain methods of securing total anæsthesia have been devised and one method—Jonnesco's—of anæsthetizing any part of the body.

Spinal anæsthesia is, like other forms of anæsthesia, still short of perfection, but at the present time we are in possession of drugs which perform for us a chemical dissection of the nerves. It is not too much to hope that the future holds an even more perfect selective local anæsthetic.

I can see the patient in the future being operated upon in full consciousness, while his central nervous system floats in an ambient bath of dilute innocuous local anæsthetic shutting off only pain from his perception.

Discussion.—Dr. A. L. FLEMMING said that due prominence should be given to Mr. Dickson Wright's doctrine "that a patient who was too ill for a general anæsthetic was not a fit subject for spinal anæsthesia," because a clear understanding upon this point would dispel difficulties which were apt to occur between surgeon and anæsthetist. The mortality risk of 1 in 1,000, or even 1 in 3,000, was higher than an experienced administrator would expect with inhalation anæsthesia, in his own practice, even with unselected cases.

Sir FRANCIS SHIPWAY said he had been much surprised some months ago to hear from Mr. Dickson Wright that he preferred spinal anæsthesia for surgery of the chest and for operations even on the neck or ear. His own impression had been that since Jonnesco's demonstration in this country many years ago, spinal anæsthesia had been condemned for surgery above the diaphragm, but the line of reasoning and the results given in Mr. Dickson Wright's paper had convinced him that the whole question of anæsthesia had been reopened and that it was necessary to look afresh at the problem and consider how far spinal could replace general anæsthesia. He had himself used spinal anæsthesia for many years for genito-urinary operations on elderly and old people and had been very satisfied with it, but had never ventured to use it for operations above the diaphragm. He had substituted novocain for stovaine with improved results. There were many points in the paper which he would like to discuss, but one in particular he would ask Mr. Dickson Wright to consider. He had said that he found the lessened bleeding an advantage; had he had any trouble from reactionary hæmorrhage, and if so, could he say what steps he took to avoid it?

Mr. HOWARD JONES: Some theories relating to detail in method of administration mentioned by Mr. Dickson Wright are not above criticism. Is it possible to imagine that 2 c.c. or 3 c.c. of solution injected with force against the leash of nerve trunks of the cauda equina results in novocain being projected any distance up the canal? 18 c.c. of solution injected as forcibly as a fine needle will allow, will not go further than if injected slowly. The direction of the point of the needle must always be near a right angle to the dura in the lumbar region, and even if it could be directed upwards, the effect would be negligible. A sufficiently large dose of novocain will always find its way to the neck in the Trendelenburg position. The old theory that the disposition of injected substances may be influenced by the anatomical arrangement of the ligaments, resulting in an anterior or posterior passage of solution according to the situation of the point of the needle, is now definitely disproved.

By posturing the patient after injecting large volume hypobaric solutions, anterior or posterior roots may be affected at will, and unilateral effect on both is obtained on the side, a result of considerable importance, since the upper affected side is at the disposal of the surgeon. The heavy solutions always produce a predominant posterior root block in the dorsal decubitus. Considering first the amount of drug injected, it is necessary to remember that absorption from the subarachnoid space is only second in effectiveness and rapidity to direct intravenous injection.

Three gradations of results are recognized. First a subarachnoid regional nerve root block, variable in extent according to the amount of drug available for gravitational diffusion, which in the horizontal position is limited also by the curve of the spine; next, with increasing dose a state of universal analgesia (Gwathmey), and finally general anæsthesia due to the drug circulating in the blood.

Mr. Dickson Wright has emphasized the fact that the medullary centres can be reached only through the blood, and according to the general rule the higher centres go first. The graduated effect on nerve fibres, from the sensory to the motor, is well recognized. The spine may be injected to any extent if the solution is dilute enough to have a selective action on sensory fibres only, but the resulting analgesia may not be prolonged enough for a long operation. Jonnesco's puncture between D1 and D2 will probably come in again. A small volume of stronger solution would then suffice, and paralysis of the phrenics should not matter, unless the chest was rigid. A limited thoracic nerve-root block can now be obtained with certainty in the adult. A hypobaric solution and a tape measure are necessary. Measurements from the inter-iliac line to the seventh cervical spine, in full flexion, vary between 16 and 22 in., and both shorter and longer probably exist. All that is required is to know whether the spine is short, medium, or long, and then inject a proportionate volume of solution. The neglect of this precaution has resulted in paralysed cervical motor roots, and the 1 in 1,500 percaine solution must not be injected up to the neck.

1 % novocain dissolved in 0·25% saline may be used for this limited block, and the strength may be increased in proportion to the faith of the user in the non-toxicity of this drug. When higher percentage of novocain is used sodium chloride must be left out to the vanishing point if the hypobaric character of the solution is to be maintained. The volume dosage is the same. There will be more collapse with novocain than with percaine because of the greater blood absorption from the more concentrated solution, and the duration of analgesia will not be so long.

Mr. CHARLES DONALD said that he shared Mr. Dickson Wright's preference for novocain and its synonyms. From an extensive experience, in which careful notes and experiments had been made, he believed that the only factor which influenced the extent of analgesia to any great extent was the dosage of the drug, and that the waywardness of action which sometimes occurred was dependent on some individual factor not yet explained. Such waywardness leading to extensive analgesia was not serious if ordinary care were taken. The only positive claim he could endorse for spinocaine was a slower absorption of its novocain due to the viscous vehicle, and he had given up to 400 mgm. of novocain in this form without ill effect. He had had excellent results with strychnine-free durocaine, a compound very similar to spinocaine. He doubted if ephedrine and adrenalin were prophylactics to falls in blood pressure. The greatest safety factor was maintenance of the head-down position and too rapid a return to the horizontal at the end of operation should be guarded against, especially in the old and gravely ill, when compensation was not likely

to occur quickly. The dangers of spinal analgesia had been greatly exaggerated, and were due to its injudicious use and to lack of appreciation of the necessary care after administration.

Dr. C. LANGTON HEWER said that in his opinion the essential feature of any new method of anæsthesia or analgesia must be safety. Whilst it was academically interesting to hear Mr. Dickson Wright's technique of high spinal block for such operations as thoracoplasty, thyroidectomy and excision of glands in the neck, yet it was extremely doubtful whether it could compare in safety with well-tried methods of general anæsthesia, and until there was evidence to show that it could do so its general adoption would seem to be unjustified.

The simultaneous opening of both pleural cavities under high spinal analgesia, described by Mr. Dickson Wright, appeared to be extremely dangerous, as, unless positive pressure was applied through a facepiece or intubation tube, death would inevitably ensue within a few minutes.

Referring to spinal analgesia for operations below the diaphragm, he (Dr. Hewer) had been quite convinced of the superiority of percaine to novocain or stovaine, with regard both to low toxicity and duration of analgesia.

Mr. DICKSON WRIGHT said, in reply to Sir Francis Shipway, that he had not experienced any trouble from hæmatoma formation as a result of the use of spinal anæsthesia. In certain cases where it was essential to secure a very perfect hæmostasis as in undrained amputation stumps it was his custom before suturing the wound to administer 2 minims of adrenalin intravenously with the result that every vessel that could possibly do so spurted vigorously and a more perfectly dry wound was obtained than with other types of anæsthesia.

In reply to Mr. Howard Jones: he had tried percain but some untoward happenings had made him give it up for the present. It certainly would not be a safe anæsthetic for high operations.

Mr. Donald spoke with the authority of one who had considerable experience in this form of anæsthesia, but the statement that such well-tried substances as adrenalin and ephedrine when injected intramuscularly had no effect on the blood-pressure could not pass without emphatic contradiction.

Dr. Langton Hewer's figures were much better than those usually prevailing; such perfection in general anæsthesia was denied except to a select few. Spinal anæsthesia was easy of administration and therefore available to all, but efficient nitrous oxide anæsthesia was difficult to obtain and there did not seem at present to be skilled administrators in sufficient numbers to meet the needs of surgeons.

Section of Otology.

[*December* 5, 1930.]

Some General Aspects of Intra-cranial Complications of Aural Infection.

By GEORGE RIDDOCH, M.D.

THE first question that might be asked in regard to the subject under discussion is what symptoms and signs should lead us to suspect that intra-cranial complications may develop in cases of septic infection of the ear; and, in order to eliminate as far as possible the symptoms of the primary disease, discussion might be largely restricted to those cases in which adequate drainage has been established by spontaneous rupture of the drum or paracentesis, mastoidectomy, or operation on the internal ear.

Symptoms of invasion.—In cases of acute ear disease, if, in spite of efficient drainage, the patient continues to feel ill, has no appetite, has fever with corresponding increase in pulse-rate, and complains of headache, which may be unilateral or bilateral, spread of infection is indicated. These symptoms of invasion may, after a few days, subside, and not recur, their disappearance being probably due to mildness of the infection and the patient's natural powers of resistance. Such abortive attacks are not uncommon, but as we shall see when considering the clinical course of chronic abscess, danger is not necessarily over although acute symptoms have gone.

On the other hand, the symptoms of invasion may not subside but merge into those of acute intra-cranial complications, such as lateral sinus thrombosis, extradural abscess, meningitis, and encephalitis. Nevertheless, the preliminary symptoms are the same in both groups of cases, and their importance as indicating extension of infection can hardly be over-estimated. The fact that they frequently disappear and are not followed by further complications does not alter their possible significance. They should, because of the danger of chronic abscess, constitute a warning that all may not yet be well, and should demand periodic examination of the patient for at least some months.

The same general symptoms of invasion can also often be traced in the histories of cases of chronic aural discharge, in which intra-cranial complications have arisen. As with acute otitis or mastoiditis, when they are merely preliminary to the development to some acute complication, such as meningitis, they are lost sight of in the general picture. But with chronic complications such as cerebral abscess, they are often neglected, partly because they may have occurred weeks or months before the abscess declares itself, or because, being transient, they have been diagnosed as an attack of influenza, or the result of temporary blockage of the aural discharge.

Acute intra-cranial complications.—Of the many different complications that may immediately follow the symptoms of invasion and develop acutely, I propose to confine my remarks to a few only.

Lateral sinus thrombosis.—The appearance of a swinging temperature, with shivering or definite rigors, and tenderness over the jugular veins, are the classical indications of this condition. Sometimes, however, the clinical picture is less clear and additional evidence would be of the greatest help. This can sometimes be afforded by Queckenstedt's test, which gives positive findings of value if the suspected sinus is blocked by a thrombus. The test consists of ascertaining whether, with the patient lying on his side and in the horizontal position, the

pressure of the cerebrospinal fluid, as measured by a manometer attached to a needle inserted into the lumbar theca, is raised by jugular compression on the affected as on the non-affected side. No rise of the fluid in the manometer indicates complete blockage of the sinus, but a mural thrombus would give a less complete result.

Extra-dural abscess.—The diagnosis of extra-dural abscess is notoriously difficult, especially in cases of acute otitis media and mastoiditis before drainage has been established, for the symptoms are overshadowed by those of the aural condition. With pus under tension in the middle ear and the drum intact, pain is referred not only to the ear but also to the regions of the skull above and behind it, but incision or rupture of the drum immediately relieves the headache as well as the earache. As regards mastoiditis, Dr. Symonds has told me that he doubts whether uncomplicated mastoid disease is associated with the spontaneous complaint of headache, although tenderness to pressure is an almost constant and very important sign. If that is so, it is a clinical observation of the greatest help, for if the middle ear is being adequately drained, and there is no evidence of involvement of the internal ear or mastoid cells, persistence of unilateral headache, varying in intensity, and especially if associated with tenderness of the skull to pressure or percussion in front or above the ear or behind the mastoid, should raise suspicion of the presence of an extra-dural collection of pus. An abscess confined to this situation does not give rise to focal or general signs of cerebral compression.

Meningitis.—I do not propose to describe the clinical picture, familiar to all, of generalized meningeal inflammation. The significance, however, of the condition usually called serous meningitis might be worth a moment's consideration. Personally, I feel strongly that the term "serous" ought to be given up, for it has no pathological meaning, and obscures the issue. There is only one form of meningitis that is due to extension of septic infection. It may be mild or severe, localized or general, but in each case it is caused by pyogenic organisms involving the meninges directly. When the infection is slight and of low virulence, no organisms are found in the cerebrospinal fluid, although other changes, such as increase in mononuclear cells, are present. If the primary source of infection is dealt with, and there is no abscess in the brain, meninges or extra-dural space, the meningitis frequently clears up, and is then labelled—wrongly, I believe—"serous meningitis," whereas in reality the case is one of mild pyogenic meningitis. The absence of organisms in the cerebrospinal fluid drawn off by lumbar puncture is of great prognostic value. For example, when brain abscess or mastoiditis is associated with meningitis the question arises as to whether it is worth while operating to drain the pus. Most aural surgeons will, I think, agree that it is, provided that organisms cannot be found in any numbers in the spinal fluid.

Localized non-suppurative encephalitis.—In his excellent paper on "The Diagnosis and Localization of Cerebral Abscess" [1], Dr. Symonds again drew attention to those cases in which, although the clinical picture strongly suggests cerebral abscess, yet the condition clears up spontaneously. They are not common, but each of us must have had some experience of them and been surprised at the end-result. The following is an instructive example of this puzzling complication:—

A woman, aged 56, early in January, 1929, complained of pain behind her left eye, for which no apparent cause could be found by an ophthalmic surgeon. Soon afterwards she had an attack of influenza, followed by acute pain in her left ear, severe vertical headache and post-nasal discharge. The aural surgeon who examined her on January 17 considered that the headache was due to sphenoidal sinusitis. She had also, however, acute otitis media, with a bulging drum, which was not then incised. Her temperature at this time was at most 99° F. The ear became more painful, although the headache diminished, and the drum did not burst. On January 24 there was some tenderness over the left mastoid, which was

opened, but granulations only were found. The surgeon exposed the dura in the middle and posterior fossæ and examined the lateral sinus, but they appeared to be normal. On washing them out both sphenoidal sinuses were found to be clear, but the antra were full of thick creamy pus. After these operations the temperature rose a little, and on January 30 the patient had a slight rigor. On February 3 the lateral sinus and the dura were again explored and the dura in the middle fossa was incised, with negative results. On February 4 she was dull mentally and slightly aphasic, with a temperature of 100° F. On February 6 the cerebrospinal fluid was examined and found to be normal. Total and differential blood-counts were within normal limits. The Wassermann reaction in the blood was negative. On February 8 she was examined by Sir Percy Sargent, who found that she had difficulty in naming objects, and that she made mistakes in writing. He explored the left temporo-sphenoidal lobe, but failed to find pus. Intra-cranial tension was normal. A sample of cerebrospinal fluid drawn off immediately after the operation, was clear, with an albumin content of 0·03%, a slight excess of globulin, 24 polymorphonuclear leucocytes per c.mm., and no organisms. During all this time headaches with occasional vomiting had continued, along with a temperature of about 100° F., and an irregular pulse. On February 16 pus was discharged from the external auditory meatus for the first time. When I saw her on February 19 she was drowsy and uncoöperative. Because of the aphasia, which consisted mainly of a difficulty with names, it was not easy to understand what she said. There was slight papillœdema in the left eye only, and slight right hemiparesis with corresponding reflex changes. The dura was not tense, and because of this and the negative findings at the exploratory operation eleven days before, further operative interference was not advised. She was brought to London where she was under observation by Sir Percy Sargent and myself. Since there was tenderness of her left frontal sinus, an X-ray film was taken and the left sinus was found to be a little denser than the right. Mr. William Morris, however, considered that there was no pus, although the lining of the sinus was thickened from inflammation. She gradually improved in regard to both general and focal signs and on February 22 her temperature was normal. The dura was never tense. When she went home early in March, the fever, headache and vomiting had been gone for some time, the swelling of her left optic disc had subsided, her speech and power on the right side had greatly improved. Her mental condition, although better, was, however, not quite normal, for she was suspicious and difficult to manage. Her convalescence was uneventful and recovery complete. On December 19, 1929, I saw her again on account of pain in her left ear and forehead due to recurrence of the frontal sinusitis, for the floor of the sinus was tender and the eye was red. At that time, apart from complete deafness in her left ear and lateral nystagmus, I failed to find any other abnormal signs. Her speech and mental functions were perfect. Her doctor reported the other day that she has since remained perfectly well.

In this case, which I regard as one of localized non-purulent encephalitis of the temporo-sphenoidal lobe, the signs pointed clearly to abscess, except for absence of bulging of the dura, which I think is an important negative finding, and may be helpful in similar cases. At the same time, the differential diagnosis, on the clinical evidence, is at present impossible, but a careful study of the condition may reveal points of distinction. Exploration with a brain needle, preferably through a non-infected region, as suggested by Cairns [2] must, in such cases, be used diagnostically, and when it is being carried out the tension of the dura should be noted. There is apparently no definite pathological evidence available as to the nature of non-suppurative encephalitis. For the present we must assume, with Symonds, that the inflammatory process becomes arrested at the pre-suppurative stage as the result of mildness of the infection and the patient's resistance to it. It would thus be on a par with mild or so-called " serous " meningitis.

That apparently permanent recovery from non-suppurative encephalitis does occur should not, however, blind us to the possibility of there being a small chronic abscess, which might later light up. All cases should therefore be under suspicion for at least a year.

Meningeal abscess.—A little time may profitably be spent in considering " localized purulent meningitis," which Symonds [1] has called " superficial abscess," but for which " meningeal abscess " might be a better term. As he says, for some unknown

reason, the infection in the route from ear to brain is stopped at the level of the leptomeninges, and forms pus, which is shut off, so that the infection is prevented from spreading throughout the subarachnoid space. The brain is affected only superficially. He has described two excellent examples of superficial abscess over the temporo-sphenoidal lobe, which were successfully diagnosed and drained, and referred to the occurrence of the same condition over the cerebellum, and the difficulties in diagnosis when in this situation. I may be allowed to describe a case of this kind, since meningeal abscess as a clinical entity is not fully recognized.

F. G., male, aged 30. Admitted to the National Hospital, Queen Square, September 20, 1929. Thirteen years before, his right leg had been amputated because of "sepsis." Three years before admission, a rib was resected for the same reason. About this time he had pain in his right ear, without discharge, and there was swelling "below his right eye." Two weeks before admission, when cleaning his car in the sun, he had pain in his head and right eye whilst stooping. An ache developed behind his right ear, and on the following day he was unable to go to work because of giddiness. The headache increased in intensity up to four days before admission, since when it had slightly diminished. At times he had been delirious, calling out, singing and clutching the bed-clothes, but at other times he was quite sensible. There was, however, an almost constant ache on both sides of his head, without throbbing. During the short periods of freedom he was aware of pain behind his right ear, which was not severe. There was no history of twitching, convulsions or abnormal sensations in his limbs, but his temperature had been raised. On examination the patient lay still, holding his head with his hands, obviously in severe pain. He appeared to be above the average in intelligence. His memory was good and he was coöperative. The nasal margins of the optic discs were a little blurred, and the veins were full. There was fine nystagmus in all directions, the quick component being in the direction of fixation. All the facial muscles on the right side were almost completely paralysed, and he was deaf in the right ear, bone conduction being greater than air conduction. The functions of the cranial nerves were otherwise normal. There was no weakness or dystonia of limbs, and repeated movements were well performed by both upper limbs, but the right upper limb could be bumped aside a little more readily than the left, and the finger-nose-finger test was carried out a little unsteadily by both arms. Reflexes and sensibility were unimpaired. There was, however, marked rigidity of the neck, although Kernig's sign was negative. Heart, lungs and abdomen were clear. The white cell count was normal. Osteitis, labyrinthitis and extra-dural abscess were suspected. On September 20, the right mastoid and middle ear were explored, and the dura was exposed in the middle and posterior fossæ, but no pus was found. On September 23 it was noted that the temperature had been as high as 103° F. for the past few days. The patient complained of pain in his right ear with a tendency to shoot forwards. The nasal margins of the discs were blurred, especially on the right side, and there was very marked nystagmus, coarser to the right. No other possible cerebellar signs could then be found, but on September 24 they appeared and more on the right side. His right hand was clumsy, and his right upper limb hypotonic and unsteady when outstretched. There was also incoördination of this limb which performed repeated movements badly. Cervical rigidity was not so marked as before, but headache was very severe. The following changes were found in the cerebrospinal fluid: cobweb coagulum, 510 cells per c.mm. (45% lymphocytes, 50% polymorphocytes, 5% large mononuclears), total protein 0·16%, Nonne-Apelt and Pandy tests positive, chlorides 0·685%, glucose 0·066%; no organisms in films or growth on culture media.

The diagnosis of right cerebellar abscess was made. That evening, the right lobe of the cerebellum was exposed and explored, but no abscess was found. On September 25 the respirations became slow, and the pulse was 80; on lumbar puncture, the cerebrospinal fluid was found to be turbid and under a pressure of 300 mm. The patient died. On post-mortem examination, a collection of greenish-yellow pus was found in the region of the right cerebello-pontine angle, the brain tissue at the junction of pons and medulla being inflamed and infiltrated with greenish pus. No deep abscess was present in the cerebellum or elsewhere. There was, however, an erosion of the bone extending downwards from the internal auditory meatus to the lower edge of the petrous.

One of the mistakes that was made in this case was failure to examine the cerebrospinal fluid before clear cerebellar signs appeared. The negative results from exploration of the ear and extra-dural space, in the presence of severe headache

fever, neck rigidity, and blurring of the optic discs, led us to suspect an intra-cranial abscess which, on the indefinite evidence, was not localized, although increase in the nystagmus should have been given more weight. I considered, probably wrongly, that the early nystagmus and the giddiness were labyrinthine in origin, whereas, in the light of later events, they were more likely due to the increased accumulation of pus on the surface of the right cerebellar lobe. Early lumbar puncture would have revealed abnormalities in the fluid, evidence of sufficient definiteness to indicate exploration of the posterior fossa. When the operation was performed and no cerebellar abscess was discovered, in view of the clear evidence of the presence of local pus, search should have been made for it in the cerebello-pontine angle.

Chronic intra-cranial complications.—Chronic abscess.—It is a lamentable fact that intra-cranial abscess is often not suspected, in spite of a history of aural infection, until general symptoms of raised pressure or focal signs of a gross and obvious kind have developed, and even then, too often, a wrong diagnosis is made, as the records of any hospital will show. This diagnostic error is common, instead of being infrequent, much more because of faulty investigation of the patient's medical history than because of want of expertness in locating the site of the lesion. And it is in the case of chronic abscess, to which I particularly wish to refer, that the evidence provided by the history is so often of the utmost importance in giving the clue to the nature of the lesion. Once suspicion is aroused that an abscess may be the cause of the general and focal abnormalities, examination of the cerebrospinal fluid will provide additional facts of great importance in the form of increased protein and cell-count. In dealing with this subject I should like again to consider the indications which ought to make us suspect that an abscess may develop or is developing within the brain, rather than to concentrate on the signs that point to its situation. Going back over the histories of cases of proven brain abscess following aural infection, one is struck by the great frequency of occurrence, sometimes immediately after mastoidectomy, of a transient illness of a general kind that is often looked upon as trivial. The symptoms may possibly be those of invasion, or spread of the infection inwards, and may complicate either acute or chronic infections of the ear or mastoid. There are at least three possible consequences of the appearance of such symptoms—(1) the almost immediate development of acute meningitis, encephalitis or lateral sinus infection, (2) permanent recovery, and (3) the formation of a chronic abscess. Encapsulated pus may undoubtedly lie "latent" within the brain, more often in the temporal lobe, especially the right, than in the cerebellum, for many months or longer, during which time the patient leads an active and apparently normal life. Examples can be recalled by each of us. But even in those so-called "latent" cases, careful investigation more often than not will reveal a story in which symptoms resembling those of invasion are followed by periodic short phases of poor health, discomfort in the region of the previously affected or still discharging ear, or paroxysmal headache of unexplained origin. In brief, careful historical studies would compel us to take the view that latency is only a comparative term and is acceptable only on the understanding that it signifies more or less good health during the period that precedes the onset of focal or hydrocephalic signs. Throughout the relatively latent phase, ill-health may be more obtrusive and continuous, and yet, unless the possible significance of previous aural trouble is kept in mind, the question of abscess may not be considered, since the symptoms are general and not local, and are those, in the main, of retained pus in any part of the body. But even that possibility may not be realized, chronic constipation (a common symptom of chronic abscess) or a diet that does not meet with approval (for the patient may be losing weight) or such like often being used as convenient diagnostic labels.

Careful investigation of the medical history and a greater interest in symptoms would probably prevent many mistakes in diagnosis of chronic cerebral abscess. It is a subject that requires further investigation, for information in regard to it is

incomplete. Even so, a not uncommon story is as follows. The patient says that he has been in poor health for some time past, has felt listless, disinclined for work, has been subject to headaches, which, on inquiry, are of the hypertension type, has a poor appetite, is often constipated, for no apparent reason, and may have been losing weight. His relatives declare that he has changed in temperament, for he has been irritable, moody and at times depressed. Occasionally he has felt shivery and if his temperature has been taken it is found to be 99° F., or 100° F., but it becomes normal again within a day or two. If it is recognized that he is ill and his temperature and pulse-rate are recorded for some time, the temperature, although on the whole perhaps subnormal, is apt to show an abnormally large diurnal variation. (Incidentally, if the temperature chart is turned upside down this fluctuation becomes more striking.) The pulse, on the whole, corresponds to the temperature and is more variable than it ought to be. At the same time the patient at times feels fairly well, and may continue with his business. These are symptoms of chronic mild septic absorption, and the only symptomatic indication at this stage, apart from the history of aural disease that the cause may be within the brain, is the relative prominence of headache, which may be unilateral on the side of the infected ear, or general; but, if suspicions are thus aroused, confirmatory evidence of the greatest importance is usually obtained by examination of the cerebrospinal fluid, for the pressure of the fluid, as measured by a manometer, and the protein content are often increased above normal limits, globulin is present, and there is a moderate excess of cells, chiefly lymphocytes. This incubation period precedes the development of signs of a focal lesion and of clear intra-cranial hypertension, and I would confirm Dr. Symonds' statement that severe paroxysmal headache, vomiting, papillœdema and slow pulse are late manifestations and indicate gross increase of pressure within the skull. Chronic abscesses of otitic origin ought, in the majority of cases, to be suspected before they appear. In many cases attention is first directed to the intra-cranial incidence of the lesion by signs of meningitis, which may or may not be serious, according to whether organisms are found in the cerebrospinal fluid and the pus is located and evacuated.

Chronic arachnoiditis.—There is another group of cases which are characterized by recurrent headaches, and the absence, as a rule, of any other features that might indicate the formation of a chronic brain abscess. There is no loss of appetite. furred tongue, persistent constipation or irregular temperature, and, apart from the headaches, the patients usually feel well; even although they are kept under observation for a long time no other symptoms develop. Such headaches often resemble in their clinical features those met with after cerebral contusion, which are frequently associated with local thickening of the arachnoid and loculation of cerebrospinal fluid. By analogy this group of headaches complicating aural infection may be the result of chronic arachnoiditis that had been set up by a localized mild meningitis in either the middle or the posterior fossa. It would be interesting to know whether arachnoidal changes of this sort had been found at operation.

Perhaps from the same cause more alarming symptoms may occasionally arise. Thus Cairns [2] has referred to cases of papillœdema without headache which have cleared up spontaneously. In one, however, it was followed by blindness from secondary optic atrophy, although the child remained otherwise healthy. I have no personal experience of this syndrome, the pathogenesis of which must be looked upon as uncertain until the meninges and brain have been examined either at operation or post-mortem.

REFERENCES.

[1] Symonds, C. P., "Some Points in the Diagnosis and Localization of Cerebral Abscess," *Proc. Roy. Soc. Med.*, 1927, xx (Otol. Sect., 41). [2] Cairns, Hugh, "Brain Abscess from the Point of View of the Neurological Surgeon," *Proc. Roy. Soc. Med.*, 1930, xxiii (Otol. Sect., 45).

Discussion.—The PRESIDENT said that ready help from the neurologist and ophthalmologist was most important, and he hoped that one day some neurologist would devote himself entirely to the assistance of the combined nasal, laryngeal and aural specialities.

With regard to lateral sinus thrombosis, diagnosis of the typical case was of course comparatively simple; it was the recognition of the "mural" forms and associated blood infection for which we particularly required help.

Sir JAMES DUNDAS-GRANT said that when the lateral sinus was exposed and there was no blockage, it was easy to get a fluctuation between the internal jugular vein, not exposed, and the exposed sinus; and if this was absent one could be sure there was a complete blockage below. Extradural abscess could exist without any symptoms being present. A discharge from an extradural abscess into the meatus could be recognized as such if an increased flow from the tympanum and meatus was accompanied by diminution of symptoms. There was sometimes what had been described as the "shirt-stud" abscess, i.e., when it had perforated the squamous bone and there was a large subperiosteal collection of pus outside, and the waist of it (the stud) was in the bone, the other part of the "stud" being extradural and sometimes issuing by the middle ear and external meatus when pressure was made on the mastoid swelling.

He thought otologists had decided that tenderness over the mastoid in the first week of acute suppurative inflammation in the ear indicated merely a congestion, but if it continued it indicated that inflammation was established, and that probably there was pus already forming in the superficial cells.

Another point of interest was the question of the localized superficial cerebral abscess. One or two cases had been reported to the Section in which an abscess had been found in an unusual region. He had once had a case in which the first symptom was paresis of the opposite arm, and at the post-mortem examination several superficial abscesses of the brain were discovered.

Dr. Riddoch had referred to the ponto-cerebellar angle. There had been some cases in which cerebellar symptoms had been well marked, but had disappeared when the dura mater was laid open and a puncture made in the meninges allowing the escape of fluid. In conditions in this angle one should keep in mind the labyrinthine reactions: the cold caloric test might show loss of reaction of all the semicircular canals on the affected side and of the vertical canals only on the sound side.

Dr. C. P. SYMONDS said that in most cases in which it was reasonably certain that a cerebral abscess was present, the localization, on neurological grounds, was not particularly difficult. The difficult clinical problem was that of deciding whether there was an abscess or intracranial complication present or not.

What were the symptoms and signs which corresponded with the evolution of the intracranial complication? In a case of proven abscess it would repay one to look back on the history and try to find the points which should have led one in the first place to suspect invasion. Here he would ask otologists a question: How much, in the way of pain, fever and constitutional disturbance could be allowed for, after an uncomplicated case of otitis media after drainage, or simple mastoidectomy? He would like to hear from otologists what was the normal clinical picture of post-operative convalescence in acute otitis media, or after mastoidectomy. He agreed with Dr. Riddoch that there was a tendency to regard the interval between invasion and declared cerebral abscess as a period of latency, but it was probably no more than relative latency.

Since he had read a paper before this Section three years ago he had learned to recognize a particular clinical picture, which seemed to stand by itself. He had had three instances of it, and the story in each was much the same: acute otitis media, or an exacerbation of an old otitis media, followed by symptoms indicating meningitis. When the patient was seen there was a swelling of the optic discs, which was surprising to the beholder, in view of the relatively good health and the mildness of the symptom picture. Lumbar puncture showed a gross increase of intra-cranial pressure, though the cerebrospinal fluid would be found to be normal. If an exploratory operation was undertaken the dura would be found to be under very great tension. An exploratory puncture in the middle fossa would enter the lateral ventricle at no very great depth, and the cerebrospinal fluid from the ventricle would be found to be normal. There were no localizing signs of cerebellar or temporal abscess in his three cases, and the patients made a complete recovery.

[Dr. SYMONDS then quoted the details of an interesting typical case seen by Mr. W. M. Mollison and himself in September, 1928.]

Dr. J. S. FRASER, referring to Dr. Riddoch's criticism of the term "serous meningitis," said that Dr. Riddoch might, if he preferred, call it "mild pyogenic meningitis." In cases especially of extra-dural abscess in the posterior fossa, benign serous meningitis was met with. There were other cases of malignant serous meningitis in which the patient died before the cerebrospinal fluid had become purulent, but those were not now being discussed.

With regard to the case of superficial abscess in the posterior fossa, he asked how the cerebellum was explored. One method was to explore medially to the descending portion of the lateral sinus; the other was posteriorly behind and below the sinus. If the case of superficial abscess in the posterior fossa had been explored medially to the lateral sinus, the abscess about the cerebello-pontine angle would not have been missed.

He was interested to hear Dr. Riddoch mention the time-honoured textbook dictum about tenderness along the internal jugular vein; his (the speaker's own experience) was that this was not a sign of lateral sinus thrombosis. But having got into textbooks it would be difficult to prevent its continued appearance in them.

With regard to headache *qua* headache, after the mastoid operation had been performed, the patient in an ordinary case of mastoiditis did not complain of headache, but of pain on moving the head. If a patient who had had the mastoid operation had severe or generalized headache, he would suspect an intracranial complication, probably meningitis.

Dr. Symonds had given a picture which corresponded very closely to what otologists knew as Gradenigo's syndrome, i.e., acute otitis media, paresis of the sixth nerve, and intense pain over the corresponding side of the face due to involvement of the fifth nerve. It was said that this was due to localized meningitis towards the apex of the petrous bone, affecting the sixth nerve as it passed through the dura. In most of these cases the prognosis was good, though some had gone on to purulent meningitis and death.

Mr. WATKYN-THOMAS said that three days ago he saw, for the first time, a case of tenderness over the jugular vein, and in that case the tenderness was due to infected glands surrounding the vein. He did not see how mastoiditis alone could cause headache at the vertex, unless there was some dural involvement, but accessory sinus infection might be a complicating factor. In cerebello-pontine angle conditions he had three times noticed one sign, namely, the firm tucking of the head over to the side affected, the sterno-mastoid muscle not being affected; any attempt to put the head straight was much resented. With regard to the diagnosis between labyrinthine and cerebellar conditions, he thought that as the lesion advanced—when once the destruction was complete—the labyrinthine signs always tended to pass off, whereas the cerebellar signs always became greater.

Mr. T. B. LAYTON, in reply to Dr. Symonds' questions, said he thought that after an operation for acute mastoiditis all the untoward symptoms, including the pain, should have disappeared within forty-eight hours. If not, and one washed out the wound with a pint of saline the temperature would probably come straight down, otherwise a further complication should be suspected. To this there were two exceptions. Inflammation of the mastoid was not of itself a disease; it was part of a general inflammation in the upper respiratory tract, and this might cause the rise in temperature, especially if the mucous membrane of the respiratory tract and the glands of the neck were particularly involved. Secondly, general septicæmia might be arising at the time the mastoid trouble was developing; or the mere fact that one operated in an early stage of inflammation of the bone might determine the septicæmia. He did not think the tenderness over the mastoid was a symptom of inflammation of the cancellous bone and it was this that one wanted to diagnose; it was evidence that the inflammation had spread though the cortical bone and was beginning to involve the periosteum.

With regard to acute otitis media: after the drum-head was ruptured, or after paracentesis, pain disappeared at once. If pain was present next day he would begin to suspect that the bone behind the middle-ear was involved. Acute otitis media tended to get well in four days.

Thrombosis of the lateral sinus was a condition which should be left alone, as it was nature's method of arresting the spread of infection, and should only be disturbed if there was reason to believe that the thrombus itself was beginning to break down into pus. This could be suspected at the operation when there were changes in the dura, either œdema or a greyness that showed it was beginning to slough, or if in the middle of the granulations there was a small quantity of pus.

Mr. A. LOWNDES YATES said that he had sometimes gained a hint of likelihood of intra-cranial complications from the type of mastoid revealed at operation. Where the mastoid was pneumatic, pus passed more easily in an outward direction. These were the

cases which had tenderness over the mastoid owing to periostitis. In other cases the outer table was thick and the inner table was easily perforated by pus, and patients were then more liable to intra-cranial complications.

Mr. SYDNEY SCOTT said a physician might sometimes think that an otologist knew a little about the ear only and was not wide awake for other troubles. Some otologists had not forgotten all their medicine, and were still interested in some branch of general surgery, and so did look out for these cases at an early stage. When it was appreciated that the otologist might have a brain abscess to deal with, so large that it involved the whole temporo-sphenoidal lobe, extending also into the occipital lobe and undiagnosable by the physician or the neurologist, it would be seen that the otologist had his difficulties. He had seen such a case without optic neuritis, and when the dura mater was exposed there was no increase of intra-cranial pressure.

Another type of case was one diagnosed as a brain tumour for two years, but in which an encapsuled brain abscess was found in the region of the uncinate gyrus. Mastoid infections were often associated with other complications. No surgeon should overlook the possibility of an empyæma. He (the speaker) was always anxious to have not only the neurologist, but also the general physician to see his obscure and difficult cases.

Mr. H. V. FORSTER said he used to imagine that to explore with a medium-sized needle and serum syringe would not be a reliable method in the diagnosis of brain abscess, until he read two papers by Robert Lund,[1] which had impressed him with its value.

During the last 2½ years he had used this method in five such cases and found a brain abscess. All the patients had recovered. The method might lead to earlier exploration for brain abscess because the degree of trauma would be negligible should a healthy brain be punctured and the presence of an abscess be excluded.

Dr. RIDDOCH (in reply) said that our knowledge of this important subject was far from complete, and it was probable that much could be gained from its study. For example, after mastoidectomy, patients whose symptoms did not soon disappear after operation should not be lost sight of, and an attempt might be made in hospital practice to keep in touch with them.

In regard to Mr. Fraser's assertion that Dr. Symonds' cases were examples of Gradenigo's syndrome, an essential difference was the development of hydrocephalic signs, such as papillœdema, which inevitably led to the consideration of abscess.

He did not regard the question of the terminology of "serous meningitis" as trivial. Why call this relatively innocuous variety "serous," since meningitis was inevitably associated with increase of fluid in the sub-arachnoid space? The term "serous" had therefore no special pathological significance, and was, in addition, inaccurate as well as a cloak that hid its infective ætiology.

Changes Occurring in the Cerebrospinal Fluid in Some Intra-cranial Complications of Otitic Origin.

By A. B. ROSHER, L.R.C.P., M.R.C.S., D.P.H.

BEFORE discussing these changes I should like to say a few words on the collection of the fluid and the tests commonly employed. Owing to the improvements of technique during the last few years the tests have become extremely delicate and reliable, but their reliability depends very largely on the manner in which the fluid is collected. About one out of every five specimens which are sent to the laboratory in which I work, has to be rejected, owing to faulty collection. I know you are all fully aware of these pitfalls and I am bringing them to your notice once again with the hope that you will never cease to impress their importance on the house surgeon or whomsoever collects the fluids.

The commonest trouble is due to puncture blood. There is scarcely a test which is not ruined by its presence and therefore it is always advisable to collect the fluid into two, three or more tubes with the hope that the latest ones will be free from it.

[1] *Acta Oto-Laryngologica*, 1927, xi, fasc. 3.

Another point of fundamental importance is for the tube into which the fluid is collected to have a solid cork (preferably india-rubber) and not a cotton-wool plug. This is essential to enable an accurate cell-count to be made in those cases where there is only a slight increase. The importance of the cork is due to the fact that the cells in the fluid soon fall to the bottom of the tube after collection, and if it contains a cotton-wool plug, in transit to the laboratory the upper layers of fluid containing no cells may be shaken against the wool, thus leaving a false concentration of cells in the fluid below.

It is essential for the tube to be sterile, otherwise the bacteriological examination will be interfered with and the sugar test will be ruined. Finally the puncture needle must be completely free from lysol, alcohol or any other antiseptic. The fraction of a drop of strong lysol produces a cloudiness closely resembling the "ginger-beer turbidity" of generalized meningitis and of course ruins all the tests.

Tests for the Diagnosis of Intracranial Complications.

The routine tests to be carried out in order to detect intracranial complications are as follows:—

(1) Cell count. (2) Total protein and qualitative globulin tests. (3) Bacteriological examination. (4) Percentage of glucose. (5) Percentage of chlorides. The minimum amount of fluid required for these tests amounts to about 6 c.c., and they should all be carried out, without exception.

(1) *The cell count.*—Anything up to three or four cells per c.mm. is regarded as normal when the Fuchs and Rosenthal counting chamber is used. They are mononuclear cells (chiefly small lymphocytes), but occasionally large ones and cells resembling large hyalines of the blood are observed. Polymorphonuclear cells only occur in pathological fluids.

(2) *Total protein and globulin.*—The normal amount of total protein is usually taken as 0·025% (25 mgm. per 100 c.c.). Slight or moderate increase up to 0·1% is common in disease, but great increase (from 0·1% to 0·5%) is rare. Until recently, the detection of globulin was taken as a sufficient indication of an excess of protein, but this is inadequate, since sometimes there may be a large globulin increase with only a slight excess of albumin and vice versa. In order to examine more fully the distribution of these two protein fractions it is better to combine the qualitative globulin test with an estimation of total protein.

(4) *Glucose.*—The normal limits vary from 0·045% to 0·085% (45 to 85 mgm. per 100 c.c.). The percentage rises with the blood-sugar in diabetes and also a slight rise occurs with increased intracranial tension. The reason for the latter is at present obscure. Decrease or disappearance indicates the invasion of the subarachnoid space with certain microörganisms and their products, providing of course, that the fluid has been kept free from external bacterial contamination.

I understand from Dr. Jocelyn Patterson, the biochemist in our laboratory, that the rough guide afforded by Fehling's test is unsatisfactory and has been superseded by the methods employed for estimating the amount of sugar in the blood. This may account for some of the criticisms that have been raised as to the value of the sugar findings. Dr. Patterson regards the glucose test as an important item in the examination of the fluids under discussion to-day. He says that its value would probably be further enhanced if a blood-sugar estimate was made at the same time, as normally the level of the sugar in the cerebrospinal fluid is primarily dependent on the blood-sugar level.

Chlorides.—From 0·72% to 0·75% (720 to 750 mgm. per 100 c.c.) are taken as normal limits. They are fairly constant and any fluctuation above or below these levels can be regarded as pathological. Generally speaking, if they are above 0·75% renal deficiency is indicated, but when there is a reading of 0·68%, or below this, a diagnosis of generalized meningitis is suggested. In tuberculous meningitis the

percentage is lower than in any other condition, and 0·5% can be regarded as pathognomonic of the condition. This lowering of chlorides is bound up with the lowering of plasma chlorides in these conditions, but the reason for this drop is unknown.

Changes to be Observed in the Cerebrospinal Fluid and their Significance in Intracranial Complications of Otitic Origin.

I have been asked to concentrate my remarks on the changes to be found in the cerebrospinal fluid in the conditions known as meningism, serous meningitis, localized meningitis, and generalized meningitis.

As regards the changes to be found in these conditions, I find that I have been drawn into a distinctly controversial matter. We have the terms "meningism," "serous meningitis," "sympathetic meningitis," and so on, and I have the greatest difficulty in finding out what they signify, and furthermore what changes in the cerebrospinal fluid, if any, are characteristic of these conditions.

In the latest edition of a standard textbook on otology I find the following definition: "If the fluid is under tension, but clear and sterile, and the cell elements . . . . are not found to be increased, a serous meningitis is probably present." As this did not conform to my impression of the condition, I consulted every otological textbook that I could obtain and found that the majority did not commit themselves to any statement on the subject. However, eventually I found a book which clearly stated that in cases of suspected meningitis following mastoid operation, if an excess of cells occurred in a clear sterile fluid the case should be classed as one of serous meningitis.

I was comforted by reading this, as my own impression of the findings in this condition is that there should be a moderate increase of cells and protein in an otherwise normal fluid. In other words, the slight rise in cells and protein indicates to my mind that the outposts of an inflammatory process have just reached the subarachnoid space. These outposts are chiefly mononuclear cells, but there are nearly always a few polymorphonuclear cells present, and their percentage rises as we approach the second stage, when the causative organisms appear and there is the condition which I take to be *localized* meningitis. At this stage the fluid becomes turbid and the polymorphonuclear cells predominate, giving rise to a large excess of cells (150 or more per c.mm.). The organisms and ferments from the cells usually attack the glucose, which frequently diminishes or disappears.

The protein content naturally rises, but so long as the percentage of chlorides remains within normal limits it is usual to regard the meningitis as still being localized, although bacteria and inflammatory products have been thrown out into the cerebrospinal fluid.

The third stage is reached when the percentage of chlorides goes down below 0·68%. The condition can then be regarded as one of *generalized* meningitis. Greenfield states that as long as the chlorides remain at their normal level there is hope of cure by surgical intervention.

In the case therefore of an infection spreading locally from the ear to the subarachnoid space it seems possible (with certain limitations) to obtain information as to its progress by repeated examinations of the cerebrospinal fluid, and I imagine that the changes are pretty much the same in the case of an infection spreading from the substance of the brain to the subarachnoid space. However, it is important to bear in mind that the value of the information obtained from these examinations is largely dependent on there being free communication between the cerebral and spinal fluids.

From the laboratory standpoint therefore, we can broadly classify fluids from these cases into three types, and I find it convenient to think of them as being primary, secondary and tertiary stages of a generalized meningitis, fully realizing

that the inflammatory process may be arrested between each of the stages, especially between the first and second.

In the primary or invasive stage there is a slight increase of cells and protein, but the percentage of glucose and chlorides remains normal. In the secondary stage (localized meningitis) we get a rapid increase of the polymorphonuclear cells and protein. The organisms appear and the glucose usually diminishes, but the percentage of chlorides remains normal. In the tertiary stage (generalized meningitis) the percentage of chlorides diminishes. I should be interested to know if it is possible, and if so whether it would be advisable, to classify the clinical signs and symptoms of this type of meningitis into primary, secondary or tertiary stages likewise. By so doing we could dispense with the plethora of terms to which I have referred and which have led to such a state of confusion.

Discussion.—Mr. PETERS asked how long it was before the condition of inflammation in the subarachnoid was recognized by lumbar puncture. Some years ago he saw many cases of cerebrospinal fever, and it was often forty-eight hours after the onset of the disease before a lumbar puncture could indicate a definite diagnosis.

Dr. J. S. FRASER said he was surprised at this division of meningitis into primary, secondary and tertiary, and especially at the inclusion in the secondary group of cases in which organisms were present. From the otological point of view one knew that cases in which organisms were present in films and cultures were nearly always fatal. Why was so much importance attached to the chlorides in the cerebrospinal fluid? He would have thought it would be better to take out from the secondary group those cases in which organisms were present and put them into the tertiary one.

Did Dr. Rosher consider that there was any danger of spreading a localized trouble in the internal meatus and posterior fossa downwards by lumbar puncture?

Mr. SYDNEY SCOTT said that the cerebrospinal fluid helped very little in the estimation of the seriousness of a case unless there was repeated puncture and examination. He had been surprised at the number of cases which recovered although organisms had been found in the cerebrospinal fluid.

In some subsequently fatal cases the fluid when withdrawn seemed to be normal, but the pathologist, when the diagnosis was doubtful, had made cultures and had found pneumococci.

Mr. O. POPPER said that the cerebrospinal fluid often gave valuable information in cases of suspected mastoiditis in children. The smallest increase in the number of white cells (even 3 or 4 per c.mm.) was diagnostic of acute mastoiditis. A negative finding had no value in so far as precluding such a diagnosis.

The explanation according to Neumann's law—which states that an intracranial infection of otological origin was always in the immediate vicinity of the original infection—would seem to be that a protective cellular reaction took place on both sides of the thin and vascular tegmen antri of children.

When the finding was negative it might be presumed that the main infection was not in juxtaposition with the meninges.

Mr. SYDNEY SCOTT said there was a danger in cerebellar abscess of arresting respiration by taking away too much cerebrospinal fluid. He had known patients cease breathing when too much fluid was withdrawn.

Dr. ROSHER (in reply) said that it was rare to find organisms in culture when not seen in films in cases of meningitis following ear disease. At the onset of intracranial complications the period which must elapse before pathological changes could be detected must vary. (The earliest time from the onset he had seen recorded was three hours.) One learned, by practice, to know what organisms found were likely to be due to contamination. People were apt to be content with too few examinations of the cerebrospinal fluid. If, as a routine, examinations of the fluid were made at least every twenty-four hours, more information about these cases might be obtained. There might be something in Dr. Fraser's remark as to the possibility of spreading the infection downwards, particularly in the primary stage by lumbar puncture, especially if a large quantity of fluid was withdrawn, but on the whole, as only 6 c.c. were required for all the tests, he doubted whether any harm was done to the patient by withdrawing this quantity of fluid. And it was due to the fact that it had been definitely stated in textbooks that lumbar puncture was a beneficial measure in these cases, that the present plea for more frequent examinations was made.

Right Chronic Temporo-sphenoidal Abscess. Wagner's Osteoplastic Craniotomy and Drainage. Radical Mastoidectomy Five Months Later.—L. GRAHAM BROWN, M.D., F.R.C.S.

December 17, 1929.—Patient, J. H. M., male, aged 25, with bilateral chronic suppurative otitis media since childhood, complained that three days previously he had had an attack of giddiness during which he fell over.

December 24.—Left hospital with condition undiagnosed.

February 11, 1930.—Readmitted, complaining of attacks of headache, giddiness and vomiting, of three weeks' duration. Thick yellow discharge from both ears.

February 26.—Abscess of right temporo-sphenoidal lobe now suspected, though the localizing signs were by no means clear. Operation decided upon.

March 3.—Operation by Mr. R. L. Galloway, under intratracheal gas-and-oxygen anæsthesia. Wagner's osteoplastic craniotomy performed. A large right temporo-sphenoidal abscess was located and evacuated by means of the cannula of a large brain-exploring needle. The wound was closed after exteriorizing the cannula through the bone-flap, and the abscess cavity was further cleansed by four-hourly injections of eusol through a fine Carrel tube inserted into the cannula and left in situ. Wound healed.

April 10.—The exhibitor saw the patient for the first time. The discharge from the right ear had ceased, but there were symptoms of renewed intracranial pressure.

April 12.—Secondary drainage of temporo-sphenoidal abscess performed by Mr. Galloway, and 1½ oz. of thick, gelatinous pus was evacuated. Cleansing of the cavity was effected as before by means of the Carrel tube method. Patient now made an uninterrupted recovery.

August 14.—Right radical mastoidectomy. No macroscopical evidence of the path of infection to the brain could be seen.

November 27.—Patient remains well. The right ear cavity has not completely epidermized, and there is a slight discharge.

Discussion.—Mr. H. V. FORSTER said that in the drainage of brain abscess by the conservative method he used the finest rubber catheter at the first insertion and he had become enthusiastic about this method, as he had had a series of five consecutive cases which recovered after that treatment. He favoured conservative drainage through the untraumatized dura. In exploring for the abscess with the needle he was in the habit of drawing off the pus into a serum syringe and he had drawn off as much as 2½ oz. There seemed to be no ill-effects. He did not think the catheter acted as a drain-pipe but that it served for drainage at its circumference.

Mr. GRAHAM BROWN (in reply) said he was only called in late after the operation, when secondary symptoms of intracranial pressure had arisen. Further drainage was carried out by the surgeon (Mr. Galloway) using a needle $\frac{3}{16}$ in. in diameter, introducing through the cannula a fine Carrel tube. Into the brain cavity was injected a small quantity of eusol, four-hourly, until there was healing. The question was whether operation should not be carried out through an aseptic area, rather than through a contaminated tract. How could one avoid a spread of meningitis by operating? If one could go through the tract without breaking down the adhesions, there should be a reasonable chance of curing the abscess, but if one could not see the exact tract, there was the danger of a breaking down of these adhesions and hence meningitis, which was invariably fatal. Therefore why not go through an aseptic area and deal with the focus later? Many more cures might be brought about in this way. Mr. Galloway turned down a large osteoplastic flap over the temporal area, then incised the dura, and evacuated the abscess by means of a large exploring needle. He then removed a piece of bone from the lower margin of the bone-flap and brought the cannula of the exploring needle to the surface through the corresponding scalp area.

Mr. SYDNEY SCOTT said that in the ordinary case of otitic brain abscess, diagnosable before operation, it was preferable to follow the path of infection, to explore and drain the abscess. Lives had, however, been saved by operating directly on the brain without previously opening the primary seat of infection. Where, for certain reasons, the path of infection was not followed, and the brain was exposed by radiate incision of the dura mater, when

pressure was high, the brain would bulge through the opening, and drainage could be effected without affecting the space between dura mater and arachnoid. He was afraid of the small incision in the dura mater, for no pus might be seen and yet an abscess might leak into the dural-arachnoid space. Ballance had described experiments to show that large exposure of dura mater did not produce decompression of the contents unless the dura mater also was incised.

Mr. GRAHAM BROWN, answering Mr. Scott, said Mr. Galloway did see a bulging of brain, so that he must have opened the dura mater sufficiently to realize that there was an abscess.

Mr. J. S. FRASER said the risk of infection and production of meningitis could be avoided to some extent by the Le Maitre method. He had recently had a case of temporal lobe abscess in which the bone of the tegmen was greenish-grey. On removing it there was a collection of pus between the roof of the antrum and the dura. He put in a Cushing pus-seeker and evacuated two tablespoonfuls from an abscess. No more pus had since come away. As there had since been progressive improvement he was leaving the case alone.[1]

Intracranial Division of Auditory Nerve for Relief of Tinnitus.—A. DICKSON WRIGHT, M.S.

R.O., male, aged 49. History: 1922. Treatment for diabetes which has continued till the present. 1929: Tinnitus developed in the right ear and became gradually worse. January, 1930: Operation through mastoid region with a view to checking the tinnitus. The results of this operation were: (*a*) suppurative otitis; (*b*) total deafness on right side; (*c*) total right facial palsy; (*d*) intensification of the tinnitus.

November 4, 1930: Condition on admission to St. Mary's Hospital. The noises were affecting the patient's mentality, he was sleeping very little and there was a suggestion of suicidal tendency. The tinnitus was of the nature of church bells, twittering birds and, occasionally, human voices. There was a foul discharge from the right ear, which was completely deaf. Diabetes mellitus was severe, the urine containing 4% and the blood 0·56% of sugar, and 40 units of insulin daily were required to control it. Vertigo and nystagmus were both absent. November 15, 1930: On the suggestion of Dr. Wilfred Harris, the eighth nerve was divided intracranially. Local anæsthesia was used and the nerve exposed through the posterior fossa with backward retraction of the cerebellum. There were some meningeal adhesions, possibly the result of the previous operation. The auditory and facial nerves were separated and the former divided. Convalescence was only complicated by the diabetes, which for a short time became difficult to control, but the patient was able to sit up on the fifth day.

As a result of the operation the tinnitus is almost completely abolished, the patient sleeps well and his mental condition is much improved.

FURTHER REPORT OF CASE PREVIOUSLY SHOWN.

Right-sided Cerebellar Abscess and Thrombosis of Lateral Sinus and Jugular Bulb. Operated on in November, 1905, and shown at a Meeting of the Otological Society on February 5, 1906.—Sir JAMES DUNDAS-GRANT, K.B.E., M.D.

Complete recovery took place and the patient served in the R.F.A. during the whole of the European war.

When formerly tested, rotation to both sides was followed by nystagmus, but no past-pointing, falling or giddiness. Caloric test (cold air) to test the *right* horizontal canal, produced no nystagmus after 1½ minutes, no giddiness or past-pointing. When applied to test the *left* horizontal canal, there was slight nystagmus in 28 seconds, no past-pointing but slight tendency to fall to left. With the galvanic test to each side there was nystagmus.

[1] *Postscript*, 13.12.30.—Case still doing well, fourteen days after operation.

United Services Section.

[*November* 10, 1930.]

Air-sickness and Sea-sickness.

By Group-Captain MARTIN FLACK, C.B.E., M.B., B.Ch.

[*ABRIDGED.*]

AIR-SICKNESS and sea-sickness have certain factors in common; they differ in the relative importance of the various factors. In both maladies the following may play a part: (1) Undue stimulation or hypersensitivity of the vestibular apparatus of the internal ear; (2) dilemma between visual, labyrinthine and deep-muscle sensations, accentuated by induced disturbance of ocular muscle balance; (3) physical factors such as stuffy atmospheres, smells, and lack of adequate ventilation; (4) anticipatory nervous anxiety; (5) the general health of the subject at the time of exposure to uneven movement, including the tone of the abdominal musculature.

AIR-SICKNESS.

No reliable statistics exist as to the real degree of prevalence of this malady. It would be of service if statistics were available as to the proportion of sick passengers arriving at air ports, especially if comparison were possible between those arriving over practically the same routes under more or less the same air conditions, in different types of machines. It is difficult to estimate the extent to which anticipatory nervous anxiety is responsible in inducing air-sickness, but it undoubtedly plays a considerable rôle, especially when combined with the defective ventilation of the cabin. That such defective ventilation is the great cause of air-sickness among passengers can be gauged from the fact that pilots who have been accustomed to flying in open machines, have had their first experience of air-sickness when in enclosed machines. Attention was first directed to this during the occupation of the Rhine Territory when pilots who had been flying in the war without trouble, were air-sick when flying from Cologne in a standard type of war machine to which a cabin had been fixed. Several pilot-passengers who have felt symptoms of nausea within the cabin have testified that all such symptoms have disappeared when they have been permitted to fly in the open with the pilot; thus indicating that whatever the atmospheric conditions prevailing, the turning point in causing symptoms appears to be enclosure within a cabin—a view confirmed at the recent International Air Congress at the Hague by several doctors of considerable flying experience.

Investigation shows that the ventilation of aeroplane cabins needs improving and the Air Ministry have put forward several recommendations to this end. Aeroplane cabins at present ventilate from back to front and tend to get "stuffy" in certain parts, while remaining cold in others. If a person opens the window near him it does not cool him, but the incoming air causes inconvenience to the

passenger in front. If a front passenger vomits, his fellow-passengers see him vomit; if a back passenger vomits, the smell of vomited material passes forward to those in front.

The investigations in respect of the ventilation of cabins have been carried out by means of the kata-thermometer and the ordinary thermometer. From the readings obtained by these at foot and head levels, the comfort factor " H," and the air velocity at various points of the cabin have been determined.

From these observations it has been concluded that for adequate ventilation, giving comfort in air travel, not only should the air pass from the front of the cabin to the back, but draughts should be excluded from leaking orifices around doors and windows, except for the special provision of a gentle breeze upon the face and shoulders which the passenger can turn on and off at will. There must be no offensive smells. The temperature at head level must be cooler than at foot level, since the converse, even of a relatively slight degree, produces, with moderate to warm temperatures, a feeling of stuffiness and discomfort, with cooler temperatures, one of chilliness or coldness.

[Examples of readings in well-ventilated and badly-ventilated cabins were shown.]

The importance of proper ventilation is now being realized and undoubtedly will be much improved in the aeroplanes of the future. It is probable that the most effective system will be the admission of fresh air through specially placed ventilators, combined with an extractor system ensuring air-flow from front to back, the windows being kept closed—thus helping to exclude noise. Warm air will be admitted through specially arranged orifices at foot level.

With regard to the first factor as a cause of air-sickness, there are undoubtedly subjects with a hypersensitivity of the vestibular apparatus who will be sick owing to the uneven movements of aircraft in the air. Such subjects are usually sick under the influence of any uneven movement, such as swings, roundabouts and scenic railways and are generally also severely sea-sick. Travel in the air is smooth in comparison with travel on the sea, so that in the former the disturbance in the labyrinthine mechanism is small in comparison. It cannot be too widely known that people who are sea-sick will not necessarily be air-sick. When this is realized the factor of anticipatory anxiety will be much reduced and the prevalence of air-sickness also in consequence.

That the dilemma between visual, labyrinthine and deep-muscle sensations also plays a part is shown by the fact that all are agreed that for comfort in air travel it is imperative to give passengers as wide a view of the horizon as possible through big windows. Probably this is why the high-winged monoplane is one of the most comfortable types to travel in, since there are no wires, struts, engines or other obstructions in the visual line of the horizon when the machine dips in a " bump."

In air-sickness, also, as mentioned later under sea-sickness, the general health factor probably plays a part.

Vomit receptacles should not be prominently displayed within the cabin, and it might be well to occupy the minds of passengers by providing a booklet so that they might take an interest in the route instead of in the well-being or otherwise of their fellow-passengers.

To prevent the admission, as pilots, of candidates likely to be susceptible to air-sickness, special rotation tests were worked out in the Medical Research Laboratory of the Royal Air Force in 1922-1924. The essential part of the test is the testing of the pulse and blood-pressure—and in certain cases, ocular muscle balance—before and after rotating in a chair, with eyes open and head unsupported, ten times in twenty seconds. The results of this test may be summarized as follows:—

(i) In fit pilots, particularly those accomplished in aerobatics, rotation produces but little effect upon the pulse-rate or arterial pressures.

(ii) In subjects liable to vertigo, nausea, or vomiting, rotation produces a marked rise in pulse-rate and systolic and diastolic pressures.

(iii) In subjects liable to fainting, rotation produces a characteristic fall in diastolic pressure.

(iv) In highly-strung subjects, liable to develop an anxiety neurosis, there is a marked anticipatory rise of pulse-rate and systolic blood-pressure prior to rotation, which may or may not be further affected by rotation. This anticipatory rise may mask, or tend to mask, the response characteristic of (ii).

(v) In practice it is found that subjects may tend to exhibit a combination of abnormal responses, but the main criterion is the fact that the satisfactory pilot is relatively stable in his responses. As a guide it may be laid down that prior to rotation there should be no marked anticipatory rise of blood-pressure or pulse-rate, while after rotation there should be:—

(*a*) No undue rise in systolic pressure (20 mm. Hg or more).

(*b*) No undue fall in the diastolic pressure (10 mm. Hg or more).

(*c*) No marked widening of the pulse-pressure (by 30 mm. Hg or more).

(*d*) No undue persisting acceleration of the pulse-rate (beginning generally with an increase in rate of 36 or more per minute).

(*e*) No marked loss of equilibratory control, sweating, undue pallor, etc.

[Figures of illustrative cases were shown.]

Sea-sickness.

Dr. Maitland, of the Cunard Company, Dr. Marrack, of the London Hospital, and myself made two voyages, during which we studied the effects in those who suffered from sea-sickness, as well as in controls who did not so suffer, upon eye-muscle balance, blood-pressure and pulse-rate.[1] Of the 160 observations it was not possible to get adequate control observations in more than thirty cases. The conclusion reached was that true sea-sickness is predominantly due to the stimulation of the labyrinthine mechanism by the uneven movement of the ship. It is probable that in one group of people, vomiting results as the effect of direct reflex stimuli from the labyrinths, causing contraction of the stomach. Such people are those who under all circumstances are unduly sensitive to uneven movement. In the majority of cases of sea-sickness, however, vomiting is not thus directly induced unless one of the other factors come into play. In such there is no doubt that the second factor plays a distinct part, namely, the dilemma between visual, labyrinthine and deep-muscle sensations, for example, the visual and deep-muscle impressions being that the ship is going up, while, owing to "lag," the impression from the labyrinths is that the ship is still going down. Many people correct this dilemma by moving the head to stop the labyrinthine impressions and thus bring them more into accord with those of vision.

In this connection a new point of considerable interest has been observed. Sixty subjects, chiefly members of the crew, but also passengers who had never, or not for many years suffered from sea-sickness, were found to have good eye-muscle poise, as tested by the Bishop-Harman diaphragm. When muscle imbalance was present it was not aggravated during the rough weather when others were sick.

On the other hand, as shown in selected examples in the table below, it was found that in people who were going to be sea-sick, an imbalance of the eye muscles was induced or exaggerated. This imbalance was found to pass off as the patient recovered. The observation is of interest, since the induction of this imbalance will take place whether the eyes are open or shut, and arises probably reflexly from the stimulation of the labyrinth and postural muscles as shown by Magnus and de Kleyn.

[1] See *Brit. Med. Journ.*, 1931, i, 176.

Subject	Bishop Harman reading	Pulse sitting	Blood-pressures Systolic	Blood-pressures Diastolic	Date	Remarks
O. A.	3½	84	154	84	April 1	Following sickness
	1	78	128	60	April 8	Recovered seven days later
M. E.	2	86	120	80	March 30	Feeling squeamish
	3	82	106	62	March 31	Following sickness
	1	66	120	80	April 8	Recovered
H. M.	4	78	122	72	April 1	Following vomiting
	1½	78	130	80	April 9	Recovered
R. Mc.	4	67	102	60	March 30	Squeamish. Acetonuria few hours later
	1	84	108	76	April 8	Feeling recovered
W. S.	over 10	80	128	68	March 30	While sea-sick. No acetonuria
	10	72	128	72	April 8	Feeling "fine"
J. M.	1	66	126	78	March 30	Feeling fit. No acetone
	3	56	108	64	March 31	Marked acetone. Been sick
	1	66	120	70	April 5	Feeling recovered
J. M.	½	84	132	74	March 30	Feeling all right
	4	72	132	74	March 31	After being sick
	3½	60	104	64	April 1	" " "
	2	72	122	78	April 5	Feeling better, but not right
J. A. G.	3½	78	118	66	April 16	All right
	8	72	136	70	April 20	Beginning to feel queer
E. B.	1½	78	110	70	April 16	All right
	4	90	108	64	April 20	Thick in head. No vomiting
G. B.	3	72	110	76	April 16	All right
	6	78	112	70	April 20	Sea rougher. Not so good
V. H.	3½	78	114	78	April 16	All right
	6	90	98	58	April 20	Sea rougher. Headache developing

The part played in sea-sickness by stuffy atmospheres, suggestion and anticipatory anxiety, is well known. I have never been sea-sick, but I have been able by sheer imagination to make myself feel "queer" and moreover look "queer," on a stationary boat. The sight of a vomit-bowl is sufficient to make some people sick even before the boat has started.

The general health of the individual is of importance, since those having a tendency to gastric disturbance are more likely to be sea-sick than those who have not. The same remark applies to those coming aboard feeling "bilious" from the effects of too big a farewell banquet. Again, vomiting which would follow the imbibition of too much alcohol ashore, cannot be fairly called sea-sickness when it occurs afloat. Dr. Marrack reached the conclusion that changes in blood-sugar content, when observed, and the induction of acidosis are to be regarded rather as the effects of sea-sickness than as the cause of it.

Each case of sea-sickness appears to require special consideration on its merits. In some the pulse-rate and blood-pressure are raised at the outset; in others the first symptoms are attended by a fall of pulse-rate and blood-pressure, although, generally speaking, there is in the end the characteristic fall in blood-pressure and pulse-rate due to vagal stimulation.

There seems to be no special "blunderbuss" remedy for the prevention of sea-sickness. The most likely remedy would appear to be a drug which depresses the centres into which the afferent impulses stream, combined with large doses of alkali and bromide, and perhaps sugar and a little flavouring of alcohol. In reality, however, each case of sea-sickness requires a proper medical examination before deciding on the remedy to be employed for its prevention or mitigation.

Discussion.—The PRESIDENT said that Group-Captain Flack's paper explained some things that had previously been difficult to understand. He (the President) wondered why—if the ventilation of aeroplanes was so important yet so troublesome, they did not substitute controlled mechanical for uncontrolled natural ventilation? In an aeroplane which was otherwise airtight, a well-designed system of forced ventilation should enable the contained air to be kept at any humidity or kata-thermometer idex required, just as in a modern warship which depended entirely on a mechanical air supply.

He had not found that the young athlete full of health and "tone" was less prone to sea-sickness than the average—rather the reverse. He did not think an overdose of alcohol the night before a voyage had much effect on sea-sickness on the next day, and he was convinced that alcohol in moderation, during rough weather, was often a prophylactic—either by removing anxiety and fear of sickness, or possibly because it tended to make the subject less sensitive with regard to his position in space.

Dr. E. P. POULTON said that Group-Captain Flack's blood-pressure records were valuable, even though they were negative.

The main conclusion of the paper seemed to be that disturbance of the labyrinth was the all-important factor in sea-sickness. Apparently, however, the only proof was that many people corrected themselves by moving their heads up. But disturbance of the labyrinth was usually associated with nystagmus. Oriel did not find any nystagmus, and functional tests of the semicircular canals carried out by means of the revolving chair on people in port and during the voyage, yielded identical results.

He (the speaker) supposed that the labyrinth had been associated with sea-sickness from the analogy of Ménière's disease, but in that disease the most striking symptom was vertigo. If vertigo was so prominent in sea-sickness would not its victims talk about sea-giddiness instead?

A few years ago Dr. Payne and himself had published some observations which suggested that nausea resulted from a tension exerted on end-organs in the œsophageal wall and was caused during relaxation, when the muscle fibres ceased to bear the main tension. Further observations on a normal student suggested that the sensation of "globus" was due to a less intense stimulation. The student readily distinguished between the two sensations.

With regard to sea-sickness during a voyage across the Channel he (the speaker) repeatedly experienced nausea as the ship went downwards, and it disappeared as quickly afterwards. When he crossed to America in 1929, he tried, with some physiological friends, to make some observations on sea-sickness. He agreed that the chemical changes were secondary; though it must be remembered that they were observed before the onset of vomiting itself. At the end of the voyage they used the children's swing and swung various passengers backwards and forwards. All who were tried felt nausea and sinking at some stage of the swing excursion, fitting in with the view that visceral tension was a factor. The sensations were particularly marked when the subject was hungry; they were more difficult to obtain after dinner. It was well known that hunger had much to do with sea-sickness. As the œsophagus and stomach were suspended on a bony framework, all sorts of accelerations and retardations would take place on moving up and down, and produce effects on sensitive end-organs, and the whole of the nausea and sinking sensations could be explained in that way. If a tight bandage was worn round the abdomen, the wearer was saved from sea-sickness because the bandage largely prevented these alterations in tension. People lay down for the same reason, and it was better to be on a rolling ship than on a pitching ship.

Though important, he did not think the repeated nausea sensations in sea-sickness were the whole thing. He had experienced a feeling of tightness or "muzziness" in the head, and he was certain it was not nausea. It might be due to an ebbing and flowing of the cerebrospinal fluid as the ship moved up and down.

Wing-Commander F. N. B. SMARTT said that Group-Captain Flack appeared to have taken as the basis of his paper secondary rather than primary causes of air and sea-sickness. He (the speaker) did not think that stuffiness of the cabin was the primary cause of sickness in the majority of people who travelled by air. One could fly from Baghdad to Egypt, experiencing temperatures ranging from freezing to extreme heat, and one would be sick, irrespective of temperature, if the conditions were unfavourable. He considered that both conditions, namely, air- and sea-sickness, were due to splanchnic defect or splanchnic exhaustion, and that the primary condition necessary for producing splanchnic upset was the appreciation by the sufferer of a definite sensation of loss or disturbance of equilibrium.

People who suffered from splanchnic defects were likely to be sick when travelling by sea or air and in other circumstances. The pilot of a machine was practically never sick, except when he experienced severe bumps, and even these had to be very severe to have that effect. A doctor had asked him why that was so and he had replied that a bump was the only movement which the pilot could not anticipate or control. A pilot of aircraft, a sailor sailing a boat, or a horseman riding a horse could anticipate every movement before it occurred, and had no sensation of loss of equilibrium. The reason for this was that there was no period of muscle lag between the period of anticipation of a change of equilibrium and the change itself. If, however, one put a good pilot inside the cabin where he could no longer control the plane, he was as likely to be sick as anyone else, the reason being that there was a period of muscular lag between what was happening and what would happen next, and the pilot therefore experienced a sensation of a loss of equilibrium and so was liable to splanchnic upset. One could spin a man on the rotary chair and he would not be sick, for the reason that he was rotating round his own centre of gravity, and so there was no real upset of equilibrium. The cabins should by all means be ventilated, and a secondary cause of sickness thus removed; but a much more important secondary cause, which Group-Captain Flack had not emphasized, was the noise and the vibration of aeroplanes, not so much audible noise as the vibratory stimuli which reached the nervous system through the skeletal system. Until aircraft were built so that vibratory noises were eliminated, this chief secondary cause of nausea would remain. One had only to hark back twenty years to the old type of uncomfortable ship, with its vibrations and smells, and compare it with the modern turbine with its silence and absence of vibrations and comparative absence of smells, to see how these secondary factors entered into the production of sea sickness. People who used to be sick every time they went to sea could now travel in a turbine steamer with a prospect of comfort in reasonable weather.

Dr. HUGH S. STANNUS: As one of those unfortunate people who suffer sickness on the slightest provocation, I would suggest that there is a group of persons having a kind of diathesis, using the word rather in the sense in which it has been used by Dr. Arthur Hurst, who are particularly liable to suffer sea- and air-sickness, and I would include in this group not only all those who suffer identical symptoms when travelling in any kind of vehicle—ship, aeroplane, train, tube, car or 'bus—but also those who may develop the same syndrome, may be, when seated in a meeting hall or concert-room—hot head, cold extremities, sweating, nausea and perhaps vomiting—with anticipatory anxiety lest they cannot escape, and sometimes diarrhœa, a symptom which no one has mentioned as not uncommonly associated with sea-sickness.

The earlier history of members of this group may reveal cyclic vomiting, bilious attacks, with hypoglycæmia and acetonuria in childhood, circum-oral pallor, blushing and other vasomotor phenomena, and migraine in youth—signs of limitation of liver function—sensitiveness to fats, essential oils, tobacco and human emanations, and symptoms that have been referred to as "splanchnic." It would be interesting to know the past histories of Captain Flack's cases. Persons belonging to this group are, I believe, intolerant of mental stress or anxiety and physical strain—such as is imposed by lack of eye muscle balance, over-stimulation of the vestibular apparatus, tension of the œsophagus, or other factors introduced by travelling by sea or air.

Surgeon-Commander HAYES said that people differed greatly in respect of sea-sickness. One man could take any amount of drink and though he was sea-sick he was not incapacitated, while another would be flattened out by the sea-sickness.

Fleet-Surgeon HOME said that in 1884 that wise man v. Pettenkofer advised C. Mense, now Professor of Tropical Medicine at Cassel, then joining the German Navy, that sea-sickness was associated with binocular vision, and Mense tried tying up one eye in a storm, but found that device unhelpful in a small craft, and recovered with both eyes open (*Arch. für Schiffs- u. Tropen-Hygiene*, 1923). He ascribed sea-sickness rather to disturbance of the balancing centre or the middle ear.

Group Captain FLACK said that a reply in detail on all the points would occupy too much time. In regard to ventilation and heating his description applied to aeroplanes as they were at present. The Air Ministry was putting forward schemes to avoid factors which tended to make passengers sick and it was hoped that special attention would be devoted to the problems of heating, ventilation, noise, etc., in the new machines.

In his hurried reference to alcohol and indiscretions of diet, he did not wish to give the impression that alcohol was a cause of air-sickness or sea-sickness, but he drew attention to the fact that many went on board after taking not only a good deal of alcohol with friends, but a heavy meal also, and then ascribed their indisposition to sea-sickness, whereas they would probably have been equally indisposed after such indiscretion on land.

He apologized for not having drawn attention to Dr. Poulton's work on this subject, but it had not been possible to refer to all aspects in the time—to discuss the rôle of the vestibular apparatus alone would have taken more than his allotted time. He had not meant to implicate specially the semicircular canals, but the whole labyrinthine apparatus. Leiri and others said that this condition was more likely to be due to reflex effects from the saccule or the utricle.

Wing-Commander Smartt's remarks had dealt with air-sickness in experienced pilots and selected persons, whereas he (the speaker) was dealing in the main with air-sickness among the ordinary passengers of air travel, and in that the conditions which he (the speaker) had outlined played the predominant part. Wing Commander Smartt had said a good deal about splanchnic disturbance, but he had confused cause and effect. He (the speaker) had spoken of afferent impulses or causes and agreed that there was a splanchnic effect, a vasomotor disturbance induced in the sympathetic or vegetative system from the impulses from the labyrinths and eyes. In regard to the latter, the late Basil Lang had made an interesting experiment in trying to obtain stereoscopic cinematograph pictures. The showing of a film taken by a camera which oscillated regularly from side to side through a fixed arc, although it appeared steady on the screen, induced a feeling of nausea and caused people to get up and go out.

He (Group-Captain Flack) had included the diathesis to which Dr. Stannus referred in the physical condition of the patient. The worst case he had seen was in a woman, who had been dieted by her doctor so that she should not be sea-sick, and she was probably half-starved; she certainly had acidosis.

In regard to vomiting, there were two types of cases. One was the type in which the patient "threw up" and was better. In the other type there was prolonged nausea before actual vomiting occurred.

He had tried to show that air- and sea-sickness was a complicated condition, depending on variations of, at least, five factors, and he was sorry for the doctor who was called upon to treat patients without an opportunity of ascertaining the individual fault. He knew pilots who were only sick when they travelled in stuffy cabins. Air-sickness was not so frequent, even proportionally, as sea-sickness, because disturbances in the air were far less intensive than those on the sea; moreover, in the latter, there was a greater frequency and range of change of movement. That was why, as a cause of sickness, disturbances of the vestibular apparatus were more important at sea than in the air.

Section of Surgery.

[*January* 7, 1931.]

Simple Polyp of the Iliac Colon in a Woman aged 64.—A. E. ROCHE, F.R.C.S.

Mrs. M. B., admitted to St. Bartholomew's Hospital, December 30, 1929, gave a history of about eight months' difficulty in getting the bowels open, unless with the aid of medicine, which she previously used not to take, and also an eight months' history of a few drops of bright blood on the motions at every act of defæcation, never occurring apart from this. The stools were stated to be scanty and ribbon-like, and tenesmus to be a symptom. For one month she had had griping pain in the left hypochondrium and in the left buttock, felt two or three times a week, for a few minutes at a time, and apart from defæcation.

On examination.—There was definite tenderness in the line of the colon at the level of the left iliac crest, and nowhere else. The sigmoidoscope, which could be passed only 10 cm., revealed no cause for the symptoms

A radiological report, after a barium enema, stated that this filled the rectum and then stopped, but thereafter rapidly reached the cæcum, after passing through a narrow region in the left iliac fossa (figs. 1 and 2). The remainder of the colon filled well, the conclusion being that there was no evidence of obstruction. A second barium enema showed similar pictures, and the radiological conclusion of Dr. Simon and Dr. Wroth was that, though there was no obstruction to the flow of barium, the suspicious area suggested diverticulitis or neoplasm.

Clinically the case was puzzling, since against a diagnosis of diverticulitis was the passage of blood, and against carcinoma (the only growth that was considered) the patient's excellent condition. Nevertheless, a provisional diagnosis of carcinoma was made. On January 16, 1930, at operation a single lump was felt within the bowel; it could be pushed distally to a point in the upper end of the pelvic colon, and at this stage I thought I could feel a stalk above it. The growth, the size of a walnut, with a raspberry-like surface, and hanging by a pale stalk, 2½ to 3 in. long, and about ⅓ in. wide, was removed from the postero-internal aspect of the bowel. There were no signs of ulceration or infiltration.

Lockhart-Mummery says that,

"simple tumours are not very common in the colon." "Single polypi are occasionally met with, and are a well-known cause of intussusception; their structure is usually adenomatous and they have a long pedicle . . . and are a common precursor of cancer of the bowel."

He describes the microscopical appearances of rectal adenomata, single and multiple, the colon being always affected when the growths are multiple:—

"These polypi can be seen to consist of a central mass of typical adenoid tissue, covered outside with the ordinary columnar-celled epithelium of the colon. They are not, however, simple outgrowths or excrescences of the mucous membrane, as the submucous coat is represented. A careful microscopical examination shows that they originate beneath the mucous membrane, probably in the solitary follicles, and as they protrude into the bowel,

become covered and surrounded by the mucous membrane. In the pedunculated variety there is, as a rule, no adenoid tissue in the pedicle, which consists of a tube of mucous membrane enclosing connective tissue continuous with the submucous layer of the bowel wall."

Until I read this description recently, I did not realize that an unusual feature of the specimen now shown is the large amount of plain muscle in its pedicle. A

FIG. 1.—Radiogram after barium enema, showing filling defect in iliac colon

transverse section through the base of attachment of the polyp shows a large thick-walled blood-vessel in the midst of loose areolar tissue, surrounded by a thick layer of plain muscle bundles, containing dilated capillaries, and arranged roughly as inner longitudinal, middle circular, and outer longitudinal coats. Outside the muscle is a layer of loose areolar tissue, containing many well-formed blood-vessels, patches of extravasated blood, and a few bundles of plain muscle. Finally, there are traces of a muscularis mucosæ, a submucosa with a solitary lymphoid follicle, and a normal large intestine mucosa with goblet cells and intact epithelium.

As I have no section of the growth itself apart from its stalk, I have called it a polyp so as to be on the safe side. I have found in the St. Bartholomew's Hospital Museum only one other example of a single, simple, stalked polyp of the colon.

There is no evidence that this patient suffers from the rare condition of multiple polypi of the colon. In this affection the rectum also is commonly involved, but it was not involved in the present case, in which, in addition, the barium enema revealed only the left iliac filling defect, and in which no other polypi were seen in the incised portion of bowel, or felt from outside elsewhere in the colon. Finally, the patient remains free from symptoms.

FIG. 2.—The variability of the filling defect is suggestive of a stalked, and so movable, mass.

In the described and illustrated cases of multiple polypi, which vary in size from that of a millet seed to that of a walnut, their number is so great that, if the present patient had also had tiny seed-like polyps not palpable from the outside of the bowel, it would have been extremely probable for some of them to be seen on the exposed area of intestinal mucosa, which, however, apart from the attachment of the one big polyp, looked absolutely normal.

We may then conclude that there is a large and pleasing probability that this patient, aged 64, had only one innocent growth of the colon, of the kind more usually seen in the rectum of children.

The history of pain in association with an innocent growth, and the type and site of the pain, are interesting. Presumably it was due to, and referred from, colicky contractions of the bowel attempting to rid itself of the growth, since, after its removal, the attacks have ceased.

(I have to thank Mr. J. E. H. Roberts for permission to operate upon this patient, and report her case, and Mr. Hume, Curator of the Museum, for allowing me to borrow the specimen.)

Retroperitoneal Tumour.—HUGH WHITELOCKE, M.Ch., F.R.C.S.

Mrs. E. S. first consulted her doctor in August, 1930, because of a pain in the left groin after exertion. Examination showed a left inguinal hernia, and further routine examination revealed a large symptomless lump in the left hypochondrium, about the size of a grape-fruit, rounded, hard and smooth. It was slightly mobile, but did not push back into the left loin: it was dull to percussion. The blood-count was normal. Blood-urea normal.

A barium enema showed the splenic flexure to be pushed down by the tumour. A ureteric catheter passed 7 cm. up the left ureter, and was then obstructed, and no opaque fluid could be seen beyond this point. X-ray examination with uroselectan showed the left kidney lying in intimate relationship with the tumour, which had displaced it upwards and outwards, whilst the ureter could be seen lying to the outer side of the tumour, into which it appeared to merge at its infero-external aspect, and could not be traced further.

Exploration through a left lumbar incision revealed a large encapsulated retroperitoneal tumour, into which ran the ureter. The kidney, tumour and most of the ureter were removed. A month later 15 millicuries of radon were inserted through the lumbar incision. The patient is now perfectly well.

The pathological report is that the tumour is a spindle-celled sarcoma.

The PRESIDENT asked whether the growth was associated in origin with the adrenal on that side.

Mr. WHITELOCKE (in reply) said that the tumour was away from the adrenal and was below the kidney.

Spindle-celled Sarcoma of the Jejunum.—CECIL P. G. WAKELEY, F.R.C.S.

The specimen was removed at autopsy, from the body of a woman aged 43. The tumour projects into the lumen of the bowel, and also on to its peritoneal surface. The intestinal surface is ulcerated and injected.

Microscopic examination shows a spindle-celled sarcoma, the cells being remarkably uniform in size. There are numerous vessels in the lumen, lined by a single layer of endothelium.

Clinical history.—Mrs. Ellen R., aged 43, had always enjoyed good health, until June 28, 1930, when she felt sick; she thought the sickness was the commencement of a bilious attack. She had never suffered from indigestion at all, but had an occasional "bilious attack," which she believed to be due to constipation. After suffering from nausea for three hours, she vomited large quantities of mucus, and this was followed by severe pain across the epigastrium. The pain was accompanied by a desire to defæcate, and the patient passed what she thought was a very watery motion, but she noticed that it consisted mostly of blood.

Ten minutes later she passed a large amount of blood, per rectum, which she estimated as quite a quart. She was transferred to hospital within 24 hours of the onset of her symptoms. On admission, her pallor was noticeable, but was not so great as to suggest a severe hæmorrhage. The pulse was rapid (146) and running. The abdomen was quite soft, and there was no distension or tenderness.

The blood-count was: R.B.Cs. 1,280,000; Hb. 19%; C.I. 0·76; slight anisocytosis.

On July 8, a blood transfusion was performed, 250 c.c. of blood being given. This was followed by a rigor, and death occurred soon afterwards.

[*The report of other cases shown at this Meeting will be published in the next issue of the* PROCEEDINGS *of the Section.*]

JOINT DISCUSSION No. 2.

Section of Electro-Therapeutics and Section of Comparative Medicine.

[*December* 19, 1930.]

Chairman—Dr. J. M. WOODBURN MORISON, President of the Section of Electro-Therapeutics.

DISCUSSION ON A COMPARISON OF RADIOLOGICAL PROBLEMS IN MAN AND ANIMALS.

Major A. A. Pryer: I propose to limit my remarks to the radiology of the larger domesticated animals, chiefly the horse. Early investigators, working with primitive apparatus, obtained unsatisfactory results, and this fact, coupled with the cost of the apparatus, acted as a deterrent to further investigation.

I regard this as unfortunate, for I believe that with an up-to-date installation, radiological examination may assist in a sufficient number of cases to warrant its adoption as an ancillary means of diagnosis.

I doubt, however, whether I can bring forward anything of value as a basis for comparative discussion; the horse is rather in a class by itself, and my experience is a limited one. I am not trained in radiology, but as a veterinary surgeon I have been interested in the art for the past four years, during which period I have radiographed seventy different living horses, with a total of 230 exposures, and have made about eighty further exposures on cadavers, for calibration and experimental purposes.

The difficulties as I see them are threefold:—(1) The bulk and indisposibility of the patient, which compel us to work at excessive distances. (2) The thickness and irregular outline of most parts of the horse's skeleton, which cause variable shadows difficult to interpret. (3) The designing of suitable apparatus. The maker often has difficulty in appreciating the peculiar requirements of the horse, while the veterinary surgeon, lacking knowledge of X-ray physics, is unable to help, a trouble not likely to be overcome until some veterinary surgeon undergoes an *ab initio* training in radiology.

It may occasion surprise that I make no mention of resistance on the part of the patient as a difficulty. It is our experience that with patient handling and proper manipulation—an art in which the X-ray team must be trained—the number of horses which cannot be radiographed because they resist is very small. It is important, however, to remove any excess of high spirits by giving the patient exercise during the forty-eight hours preceding exposure to X-rays. A restricted diet is advisable for the same reason, and we impose the same preparation as would be employed for a major operation. A narcotic, in the form of one or two ounces of chloral hydrate, administered by the œsophageal tube, is useful at times, although the response to this medicament may be manifested by a motor incoördination, rather than by dulled mental perception. We plug the ears with cotton wool as a routine measure and find it indispensable in preventing muscular tremors, which are often produced by the noise set up when the switch is let in. The shoe should always be removed before radiographing the hoof, as the metal causes undesirable scattering.

Types of apparatus and technique.—Much of our early work was done with a hard tube possessing a gross focus, and the results were poor. Experience to date has shown that the best photographic effect is obtained with a transformer set, with a medium-line focus metallix tube, which will give a steady output of 80 kilovolts and 42 milliamperes: with this, for almost every part of the horse that

is radiologically accessible, we use a tube-film distance of 26 in. and an exposure of two seconds, which has been proved by experience to give the best results. Fast work is obviously desirable; attempts to employ a Potter-Bucky diaphragm have afforded no help, and a tube box capable of being moved in any direction is necessary. It seems to be a curious equine psychological fact that a nervous patient is less likely to resent an unusual-looking object being brought near to him than to be asked to approach the object.

I have no experience of radiographing horses in the recumbent position, but there are a few regions, such as the patella and mandible, in which adoption of that position is almost certain to facilitate radiological examination. I am doubtful, however, whether it will extend the field of utility as much as one may be inclined to anticipate. In many of the conditions in which the recumbent position would help—as for instance, disease of the cervical vertebræ—the nature of the suspected lesion would constitute a clear contra-indication to the forcible throwing of the animal.

Parts of the horse, radiological examination of which may assist diagnosis.—Almost every part of the horse's body is a closed book to the radiologist, with the exception of the limbs. This field may appear to be a restricted one but its peculiar importance in veterinary practice needs no emphasis. When we succeed in producing radiograms of the horse's limbs, of constant good quality, we shall have gone to a useful length.

I am unaware of any attempts, successful or otherwise, to radiograph the horse's brain, spine, heart, lungs, kidneys or bladder. Further, since the horse is fortunate enough not to possess a gall-bladder, the need for cholecystography is non-existent. By the courtesy of the Principal of the Royal (Dick) Veterinary College, Edinburgh, I have seen some films of the horse's mandible and teeth, taken with the film in the intra-buccal position. So far as I know, they contribute the first efforts in X-ray examination of this region and the results seem sufficiently promising to merit further exploration.

With regard to the radiography of the horse's abdomen. We have made several attempts, in the first place on normal animals, and secondly on one horse in which a sarcoma of the pylorus was suspected and on another in which an intestinal calculus was probable. Post-mortem examination confirmed clinical diagnosis in the first of these two cases but not in the second. Radiological examination helped diagnosis in neither, although it told us a certain amount in other ways. The technique in all cases was purely experimental. After fasting, the animals were given $1\frac{1}{2}$ pounds of barium sulphate with gum acacia and water by the stomach pump. Examinations were made at the 4th, 8th, 10th, and 18th hours. Barium shadows were seen but their localization was impossible. Peptic ulcers and malignancies of these parts are rare, as compared with those in man, and the call for X-ray assistance in diagnosis may seem far-fetched. However, it is well to know where we stand, and I think anyone desiring to explore this region further may take it that barium shadows can be demonstrated in the horse.

This year two Continental workers have published a lengthy account of the digestive processes in ruminants, as ascertained by X-rays. The investigation was more physiological than radiological, and as only small animals (young goats) were employed as subjects, no technical difficulties were encountered. The inquiry is of interest however, as denoting a new field of employment of the X-ray in veterinary science. I say a new field, because ruminants were used; Cannon, of course, used cats for a similar purpose many years ago. It is also worthy of mention that Theiler used X-rays as an auxiliary in his researches into the mineral deficiency diseases—particularly aphosphorosis—of cattle in South Africa. Valuable information was obtained from a comparison of the widths of the compact and spongy tissues of the long bones in healthy and affected animals respectively.

Now as to the radiology of the horse's limbs. Commencing above and working downwards, I know of no method of satisfactorily radiographing the shoulder, pelvis or hip. Not only is the approach to the bone which it is desired to X-ray covered by the corresponding bone of the opposite side, but the thickness of the body causes scattering which ruins the picture. The difficulty might be overcome in some cases by making the exposures from an ascertained angle, but much experimental work is necessary, and the infrequency of diseases of these regions has caused us to defer the inquiry. Much the same applies to the femoro-patellar-tibial articulation, although examination of this joint might be of more value clinically. We have found difficulty in penetration in this region, but with our present apparatus I believe this could be overcome. The shafts of the radius, ulna, tibia, and fibula are accessible, and X-ray examination is useful in suspected subperiosteal fracture. Lateral examination of the carpus is always worth carrying out. Antero-posterior views of the carpus are less easy to interpret, owing to the diffuse shadows cast, unless the rays pass perfectly straightly through the large interosseous canals. The metacarpus, metatarsus, and proximal and mesial phalanges can be well demonstrated, laterally in both limbs, and in addition antero-posteriorly in the fore-limbs and postero-anteriorly in the hind limbs. In these regions the casette is held by the hand of an assistant since mechanical holders have proved of no value. In view of this the amount of blurring due to movement is surprisingly small. There is usually a little evidence of movement over the sesamoids, but it is unlikely to impede diagnosis. Radiological examination of these regions is useful in suspected fracture, foreign bodies, osteo-periostitis, and exostoses of all kinds. Information as to the presence or absence of an arthritis—and when this exists, the degree of joint involvement—is often forthcoming.

X-ray examination of the horse's foot and the structures within it opens up perhaps the most valuable field of all. The differential diagnosis of chronic disease in this region is most difficult at times, and radiological examination may afford great help. X-ray pictures of the feet of different sound and lame horses, taken by a standardized technique, showed marked variations which can be observed with a little practice. I have drawn certain conclusions from what I have seen, but it will take much time and experience to interpret their real significance. Radiograms showing pedal osteitis are rare, whilst variations in the size and shape of the navicular bone are common. As navicular disease is incurable, we have been in the fortunate position of being able to compare clinical symptoms, radiological findings and post-mortem appearances, and we find the X-rays pretty well vindicated. To radiograph the foot, including the navicular bone, necessitates a definite technique. We have never succeeded in showing it properly in an ordinary antero-posterior position. The navicular bone affords a curious problem to the X-ray examiner. It is a small bone, say two and a quarter inches in length and three-quarters of an inch in width, situated deeply within the horse's hoof, and radiological access to it is through the much thicker os coronæ, a position comparable in some ways possibly to a postero-anterior of the human patella. The technique we employ is as follows :—

The shoe is removed, and the frog clefts are cleansed and filled with horn paste; if the clefts are not so filled, their irregular outline throws shadows which mask the navicular region. With the exposure data previously mentioned, the horse stands on a reinforced aluminium casette and the rays are centred on the pyramidal process of the os pedis, from an angle of 60 degrees. The absence of appreciable distortion has been checked by a series of mensural tests. What are the X-ray appearances of a diseased navicular bone? I suppose caries of the tendinous surface of the bone is what one would expect to see. We found some difficulty in demonstrating these carious areas. The middle cleft of the frog crosses the region one wants to see and any small foreign body, such as a fragment of grit, may throw a shadow resembling a carious area. Hence the margin of error was large, and other changes which occur frequently in diseased navicular bones were looked for, namely, (1) Increased width

of the bone, due presumably to a rarefying osteitis and evidenced by a fluffy appearance mainly at the superior border. (2) The formation of bony spurs at the extremities of the bone. These spurs are not constant but occur very frequently, and when present are the most easily demonstrated pathological change.

From examination of over 200 navicular bones I find it most exceptional to get the spurs without carious areas being present in the tendinous surface of the bone, I believe if one can demonstrate these spurs radiologically, one may diagnose navicular disease without any hesitation. The matter of the early diagnosis of navicular disease in army horses is of economic importance. To wait until clinical symptoms are sufficiently marked to warrant an order of destruction may entail feeding a useless mouth for months. I have encountered one further appearance in five cases which I cannot interpret. This is an abnormal strand of bone which appears to run from the extremity of the navicular bone to the wing of the os pedis. I call it the "osseous bridge" and have found it only in lame horses. The five cases are at present under treatment but follow-up steps have been taken and I hope to make autopsies in due course. Is this strand of bone due to ossification of a portion of the coronopedal ligament? If so, it seems to be a condition we know very little about.

Fluoroscopy.—I have been unable to employ the fluorescent screen usefully in equine practice. To see anything at all, a much higher current is needed than that customarily used, with regard to the safety of the operator.

The therapeutic use of X-rays.—I can find no records of X-ray therapy for horses, but it ought to be tried, and I suggest canker of the foot as a good subject for a starting-point.

Dr. R. W. A. Salmond: In the examination of animals there are obvious technical difficulties, rising to impossibilities in the case of the larger ones. Some time ago I was asked to radiograph the hind limb of a pigmy elephant, and a fractured bone with a fragment of bullet in situ was shown. What impressed one most at the time was the great density of the hide and soft tissues as compared with the human. The animals usually examined are less difficult. The smaller ones present few or no technical difficulties, but the larger ones may require a special radiographic table, or a veterinary operating table. The transport of the larger ones such as racehorses or valuable hunters, may be out of the question, and a portable apparatus is necessary.

Whatever apparatus is used, it should be powerful enough to allow the exposure of any ordinary-sized limb to be made in the fraction of a second with intensifying screens. This dispenses with the question of an anæsthetic and also solves many of the other difficulties in dealing with animals. It should be as noiseless as possible and no part of the tube should be brought nearer than 12 in. to the animal lest, its hairs being electrified, it should take fright. Disappointments and failures in animal radiology are, it is thought, mostly due to faulty technique. As there are no sure means of getting an animal to hold its breath, one has to depend on very rapid exposures to overcome the movements due to respiration, otherwise the shadows are blurred, especially those of the internal parts.

The most common conditions for which examinations are made are fractures and dislocations, or both combined, and foreign bodies swallowed or embedded in the soft parts. It is good practice to re-examine dislocations after reduction to make sure that they are really reduced, and it is well to remember that some swallowed foreign bodies, such as corks, pieces of stick, or sponges, may not cast any shadow. Since greyhound racing has become so popular, much work is done in diagnosing fractured toes and dislocations of the toe joints. Other uses are the determination of sarcoma, endothelioma, and tuberculosis of the long bones of dogs and cats, and diseases of the foot and limb bones in horses, also the detection of urinary calculi in dogs, the size of the pelvis in relation to breeding, and the determination of gestation.

The internal examinations, as opposed to those of the limbs, are more difficult. Compare the natural attitudes of animals with those of man. The latter quite naturally lies on his back or stands facing you, and you see the two sides of his body quite separate. When an animal is standing or lying naturally, the two sides of its body are usually more or less superimposed, but if it is put in the dorsal position and the fore-limbs drawn up and the hind limbs down you can then see the two sides separately, and examine for, say, a stone in one or other kidney. Cases are recorded from time to time in which X-rays have failed to show stone when this was present; these failures are probably due to the technique rather than to the composition of the stone. It is interesting that the chemical composition of stones in dogs is similar to that of those in man. By a barium feed the condition of pyloric stenosis in dogs can be determined, or whether a swallowed foreign body is in the stomach or has passed further on. If in the stomach, the opaque fluid will be found to obscure the foreign body. No difficulty need be experienced in getting a dog or a cat to take this meal, in fact they usually take it with a better grace than human beings do.

The thorax offers fewer opportunities. The more important smaller animals—dogs and cats—are, in this country, relatively resistant to pulmonary tuberculosis, but hernia of the diaphragm, opaque foreign bodies in the lungs or gullet should be detected, and also the less common conditions of hydrothorax, pneumothorax and actinomycosis. In the larger animals the examination is almost impracticable.

Some animal parasites are found both in man and in the lower animals, so that they are of medical and veterinary interest. When calcified or situated in an air-containing space, such as the lung, they are readily detected by X-rays. Most important radiologically are hydatid cysts, the cysts of *Cysticercus cellulosæ* and trichinosis. Hydatid cysts are occasionally found when one is radiographing the human lungs or abdomen, and show a fairly characteristic globular shadow, with usually a calcified wall. In the abattoirs these cysts are common and can be seen infesting the organs removed from cattle, sheep and pigs. Calcified cysticerci are also occasionally seen in the muscles of man as elongated opacities, about 1 cm. in length, lying in the direction of the muscle fibres. In those animals infected, namely pigs, dogs and cats, they show a similar appearance. Radiography for the detection of both these parasites is however not an economic undertaking in animals.

Another problem is that of expense. This may arise, especially in private practice, and if the economic value of an animal is taken into account, the requisite fee may be relatively high to that value, and is a limiting factor to more universal use of the rays. Fortunately there are other considerations, and when once an animal has found a place in our hearts and homes, a high value is generally placed on its life.

The interpretation of the films or screen examination should be done by a qualified veterinary practitioner. The bones of the limbs and spine of animals are different from those which a medical radiologist is seeing daily, and, if only for this reason, it is thought that animal radiology should be in the hand of veterinary—rather than of medical—radiologists, unless these latter have had some training in veterinary science. The converse of course, also holds good. For those veterinaries not conversant with the many pitfalls in radiology, they are advised that a negative opinion on screen examination alone, especially as regards a fracture, should not be relied upon. Skiagrams should be asked for, as being more accurate and constituting a permanent record.

In radiotherapy much work has been done on the action of X-rays and radium on experimental malignant growths in rats and mice, and has added to the knowledge of the effects of this treatment in allied human tumours. Bearing in mind the results in these animals and in man, veterinary practitioners might consider the treatment of sarcoma and carcinoma in dogs by similar or combined means. It is interesting to note that domestic animals are affected with practically every

variety of malignant neoplasm known to pathology. The valuable information on the action of X-rays on the different blood-corpuscles in animals has helped in the treatment by radiation of certain blood diseases in man, and might be used in the treatment of canine leucæmias.

The nutrition value of food stuffs as regards their vitamin and other essential contents, has been demonstrated by the growth of the bones in young animals and their controls, as shown by X-rays, and is being utilized in the prevention of deficiency diseases both in man and animals.

The sterilization of bitches and female cats by X-rays, when there is no question of breeding, to prevent the unpleasant events which occur at the œstral periods, might be considered as an alternative to the surgical method of spaying. Published references to this are hard to find.

While one fully realizes that, owing to circumstances, veterinary surgeons have to rely mainly on their own clinical acumen for a diagnosis, rather than on laboratory examinations—the multitude of which, it might be said, has almost befogged the medical profession—one cannot help thinking that radiology will be more and more widely used in veterinary practice as its value in suitable cases becomes better known, not only amongst themselves, but also among the laity. It will, of course, be remembered that this examination is meant not to supplant, but only to supplement, the manual examination.

In research work, radiology opens a fascinating field in the investigation of the internal functions of animals, many of which are as yet imperfectly known. Their elucidation would not only afford valuable information for veterinary science but would have a direct bearing on the better understanding of similar problems in man. The classic observations of Cannon, soon after the discovery of X-rays, on the movements of food in the stomach and intestines of the cat, were for a long time the basis of the accounts of these movements in textbooks on human physiology, and show how very closely related are the problems of human and animal physiology and pathology.

Lastly as to the future of veterinary radiology. This lies in well-equipped departments in the veterinary colleges, army veterinary hospitals, and veterinary surgeries, and also in the X-ray laboratories of institutes of anatomy and physiology, and of zoological gardens, but not in hospitals or clinics where human beings are examined. Speaking in general terms, veterinary radiology has not been developed so much as it might have been, and it is surprising to find how little reference is made to radiology in many veterinary textbooks. For further progress it is suggested that :—(1) more qualified veterinary surgeons should employ radiology, just as radiography was taken up by medical men and developed into medical radiology. (2) Every veterinary college should have a well-equipped laboratory under proper supervision. (3) Radiology should be a recognized part, however small, of the training of veterinary surgeons.

Lieut.-Colonel E. Middleton Perry: The scope for radiology in veterinary science is much less than in the sister profession, and the work is essentially much more superficial. By this I mean that we are not able to go into the finer details in diagnosis by means of radiology as in the case of the human subject.

For instance, the employment of a bismuth meal in our patients is a very difficult problem. To obtain the desired result, we cannot get our animals to swallow the meal slowly and when required, neither can we get them to keep still while the preparation is being swallowed, in order that we may watch its progress down the alimentary tract. If this could be done it would be of great assistance in ascertaining the presence of foreign bodies of low specific gravity and less opaque nature, which one so frequently finds in the dog.

The use of X-rays for the diagnosis of gastric and duodenal ulcers in veterinary surgery needs hardly be considered as I believe these cases are extremely rare in our patients.

Again, owing to the small compass of the abdominal cavity of the majority of our canine patients, many foreign bodies, calculi, tumours, or other abnormalities can be felt by palpation, and therefore resort to X-rays is not necessary, and the same remark applies to many cases of fracture of the limbs.

These few points clearly show that there is not the scope for this kind of work in our patients, that the finer points of radiology cannot be made manifest, and that for the present we must make use of the rays chiefly to help us in the diagnosis of some of the more obscure fractures, callosities and the presence of foreign bodies.

Before expressing a definite opinion as to the reading of some radiographs considerable experience is necessary, as it is often by no means easy for the uninitiated to read a negative correctly. It is advisable to have a set of normal negatives for comparison.

Dr. J. B. King: I wish to review briefly some of the problems which have been raised within the last few years as a result of the X-radiation of the ovary in animals and human beings. As early as 1905 various workers had reported that, as a result of radiographing the ovaries, there was a rapid and complete disappearance of the Graafian follicles. This work was confirmed and extended, but up to 1913, research in this direction was almost entirely histological. More recently, experimental work done with mice sterilized by X-rays has led to great advances in our knowledge of ovarian function but has at the same time, raised some interesting problems. By the introduction of the vaginal smear technique in mice, by Allen and Doisy, a reliable means has been provided for the study of the œstrus-producing ovarian hormone. While ovariectomy produces a complete cessation of the œstrus cycle, Parkes and others have shown that no such change follows a complete destruction by X-rays of all the Graafian follicles in both ovaries, and that the normal sexual cycle will develop in mice when the ovaries have been irradiated before puberty. The œstrus-producing hormone can, therefore, no longer be regarded as entirely a product of the follicles.

An interesting comparison with these results is found in the human female, where a cessation of menstruation follows treatment by X-rays of sufficient intensity to affect only the follicles. Further, however, it has been found by extended use of X-rays in gynæcological practice that, if the treatment is given during the first two weeks of the inter-menstrual period, the sterilization is immediate and no further period will follow. But if the treatment is given during the second two weeks, one, two, or even three, periods may occur. As it is now generally accepted that ovulation takes place about the fourteenth day of the cycle, there is here strong evidence of a causal relationship between ovulation and menstruation.

As has been described, X-rays have been the means of demonstrating that œstrus is not a direct result of periodic ovarian function. What then, is the controlling influence? Working from various clues, one of which was the well-known association of sexual aberration with hypophyseal disturbance, it has been established that the ovary is subject to control by an internal secretion from the anterior lobe of the pituitary body. Injection of extracts of the anterior lobe have been found to have remarkable effects on the ovary, one of which is the production of abnormal ovulation and excessive corpora lutea formation.

It has been shown that experimental irradiation of the ovaries has led to important findings, in no way indicated by ovariectomy. It is logical to expect that irradiation of the pituitary body will yield similar results. Excision of the pituitary body in rats has been done by Smith, but in X-rays we have a means by which certain cells may be destroyed, while others are kept intact. At present the anterior lobe of the pituitary body is credited with the production of two, three or even four distinct internal secretions. I suggest that X-radiation of this gland offers one of the most likely lines of experimentation. For the study of the effects of the pituitary body on

the ovary it is desirable that the work should be done on mice, and this may be possible by the use of a narrow beam of gamma-rays, produced on lines similar to those followed in the radium "bomb" treatment of human carcinoma.

Professor J. McCunn said that some time ago at his institution they had a horse which was suspected to have odontomata. The horse was cast and radiographed, and the odontomata showed up very well. Sinuses in the horse's head could also be examined, and it could be seen whether or not the teeth were normal. Often alveolitis could easily be demonstrated in the horse. The antero-posterior view of the carpus in the horse was difficult because the pisiform was in the way. At an earlier date he interpreted the shadow of the pisiform as an abscess, and took credit to himself for having effected a remarkable cure of the condition! The navicular bone was the bugbear of the veterinary surgeon; probably Major Pryer would obtain more valuable results from lateral views. Caries of this bone might occur, and sometimes it showed an erosion one-eighth of an inch deep.

Examination of the dog by X-rays was not difficult. He (the speaker) had recently had four examples of hydrothorax in that animal, and the X-ray findings had been very good.

A point had been raised about the hair being electrified. A radiologist told him that there was nothing serious in this. He found that immediately one switched on the machine, when radiographing the horse, the animal gave a jump, but was afterwards still. The rays were very useful for detecting fractures and dislocations. He thought at one time that nothing could be done in a case of dislocation of the head of the femur of the dog, an accident which, in these days of motor vehicles, was very common, but in 80% of the cases this could be reduced and the dog restored to normal with the diagnostic aid of X-rays.

Dr. Salmond had introduced the question of gestation in dogs. A good deal of work had been done on that subject, but the rays had not shown any fœtal puppies in his (the speaker's) cases, probably because of the amniotic fluid. Dr. Salmond had suggested that radiologists should concentrate on stones in the kidney and pyloric stenosis in dogs, but these were very uncommon in the dog. Gastric and duodenal ulcers also were rare in dogs. Large dogs frequently suffered from osteo-sarcoma of the lower end of the radius, and X-rays were useful in detecting this.

It was doubtful whether X-rays were of much use in the sterilization of animals; the effort was generally in the other direction—trying to make sterile animals fertile, and to this end ultra-violet rays were used. He knew one case of the kind which was a success. There was much scope for the use of X-rays in animal practice; the chief difficulty was one of finance.

Dr. A. E. Barclay said he did not think that the range of X-rays had been adequately explored in physiology and zoology, or in veterinary surgery, and there was an enormous field waiting. Just as radiology had changed human clinical medicine, so it would, in due course, change many conceptions of veterinary work and comparative anatomy. In conjunction with Mr. Harris, of the field laboratories, much work had been done on the question of vitamins as affecting the epiphysis of rats. In studying the mechanism of swallowing he had found that cats were too temperamental for the research, and dogs bolted their food, whereas hens and worms behaved quite nicely! There were many problems connected with swallowing in man on which light was thrown by X-ray investigations on animals. Textbooks on physiology stated that the act of swallowing was a succession of propulsions, beginning with the tongue, but a study of the hen's mechanism showed that it was largely accomplished by suction.

The hen was a great air-swallower, probably because of the size of its pharynx. One could also watch seeds being digested in the gizzard, and see the length of time

taken for the food to move along. The mechanism of defæcation was also interesting to study. The rectum straightened out and was drawn back over the wastage, thus bringing about its expulsion. In fact, the whole mechanism of the alimentary tract in animals was a *terra incognita* that was ripe for exploration by means of X-rays. It was a line of research that was not only of value in itself but had great possibilities as a comparative study that would help us to understand more of the mechanism in man.

Dr. James F. Brailsford: There is no question that the chief factor against the use of radiology for animals is the expense. No expense, time or skill is spared in the treatment of human beings, even when it is known beforehand that the best result will mean that the patient will be more or less of an invalid or cripple. In the case of an animal—even of a pet—its future condition is seriously considered, and if the prognosis suggests disablement it is usually decided to "put it to sleep." Personally, I think that there is a tendency to give this advice too often, without making quite sure of the diagnosis.

FIG. 1.—A periosteal sarcoma of the lower end of the left radius of a dog with an area of osteitis fibrosis cystica in the right radius.

For the X-ray investigation of animals, the plant needs to have the greatest output, because most of the radiograms have to be taken instantaneously and from a distance of three or four feet, owing to the difficulty of controlling the movements of the animal. In order not to alarm the animal the apparatus must work as

silently as possible and anything like a sudden noise from a switch or rotary must be avoided. For the X-ray examination of dogs, cats, and the legs of most animals, the films of the size ordinarily in use in a radiologist's department are sufficient, but if the chest or abdomen of the larger animals such as cattle or horses is to be examined, much larger films have to be used.

There are many conditions in animals the diagnosis and treatment of which would be helped by radiography. Many of the pathological conditions found in man

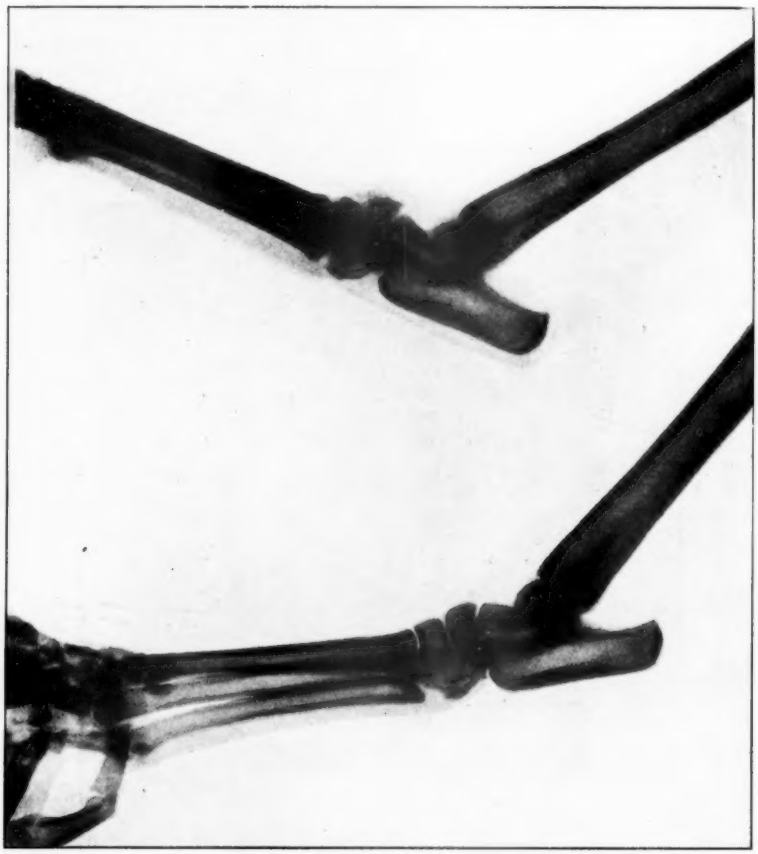


FIG. 2.—A fracture of the right scaphoid of a dog. This dog had been injured a month before and had been treated as for an injury to the right hip-joint.

are seen in animals, though the frequency may be much different and the lesions dissimilar. As an instance, tuberculosis in cattle and pigs is fairly common and is frequently seen involving not only the lungs, liver, and serous membrane, but also the spinal column. Bone disease can be shown by X-rays, and as calcification takes place earlier in tuberculous deposits in these animals, and to a greater extent than in man, the lesions would be more readily shown in a radiograph. Hydatid disease of the lung, relatively uncommon in man, but very much more frequent in animals,

could be detected. Strongyli in the lungs of animals are so common and apparently of so little importance that they are ignored, but, in the sheep particularly, *Strongylus rufescens* readily calcifies and radiograms of the lungs give a picture rather like miliary tubercle. Gas formation in the limbs of animals suffering from "black leg" or "quarter evil" could be detected by X-rays. The calcifications in the muscles of animals, due to sarcosporidia, would be shown in the radiograms.

The X-ray demonstration of lesions in the food animals, though of scientific interest, is much too costly for veterinary practice, and could only be considered in animals of great value for breeding purposes. The expense of a first-class X-ray unit and its upkeep is more than could be reasonably borne by any veterinary surgeon in general practice, apart from the time which would have to be given to a study of the technique of radiography and the interpretation of the radiograms. To attempt the work with small apparatus would only be to go to an expense which would bring disappointing results.

FIG. 3.—A large stone impacted in the intestine of a dog. The intestine is seen to be distended with gas in front. This dog had been treated as for "gastric influenza."

The greatest use, however, of X-ray investigation of animals is the detection of fractures and the position of the bones and the detection of foreign bodies. In connection with these investigations I have had the coöperation of Mr. T. N. Gold.

The actual demonstration of the site of fracture and the position of the fragments assist the veterinary surgeon in treating the condition. Often the lesion is quite away from the supposed site, and rest is given to the uninjured part, while strain is put upon the injured bone. Without the aid of X-rays fracture of the elements of the carpus and tarsus is frequently missed (see fig. 2). This occurs only too frequently in man, who can point to the site of the pain.

The fragments can be set in good alignment, and radiograms can be taken subsequently in order to see whether sound bone union has occurred.

The detection of foreign bodies, particularly those obstructing the alimentary canal, is perhaps the best life-saving use of X-rays. As with man, a preliminary

search for the foreign body must be made before any opaque meal or enema is given. If this does not reveal the foreign body, barium paste can be watched down the œsophagus and through the alimentary canal. Or, if the obstruction appears to be in the lower bowel a barium enema can be given. [A series of radiograms, illustrating obstruction in the œeophagus of a dog, only seen after thick barium paste had been given, was shown.]

I have known of a number of animals diagnosed and treated for such things as "internal distemper" and "gastric influenza," in which an X-ray investigation has revealed the presence of a foreign body (fig. 3). Cattle frequently swallow long pieces of metal wire in their fodder, and this in many cases pierces the stomach

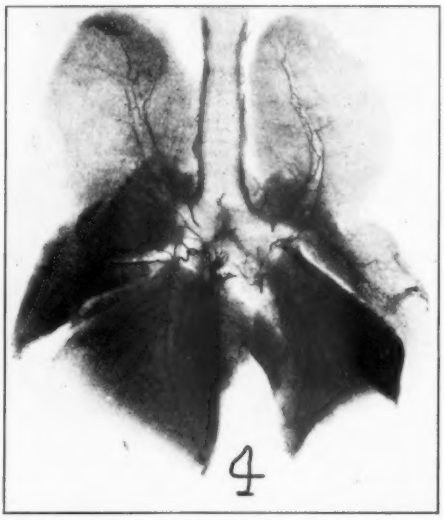


FIG. 4.—The lungs of a dog, after injection of the bronchial vessels by Professor Daly.

and the pericardium. It would be possible to detect the wire by an X-ray investigation and in this way assist the diagnosis and prognosis where the value of the animal warrants such an expensive investigation and subsequent treatment, in face of the risks of any operative procedure. Much information in comparative anatomy, physiology and pathology can be obtained by radiographic investigation (see fig. 4).

Dr. A. Eidinow said that one thing common to men and animals was the question of the lethal action of rays. Both men and animals could be burned and killed by heat. A section of the profession maintained that there was no such thing as "light stroke," but it was found possible in the laboratory to kill animals by pure visible light, excluding the infra-red rays. Animals could be killed by visible light if photo-dynamic substances were used, and also by intensive doses of ultra-violet rays, but it was necessary in that case to shave off the hair to get the full effect. Ultra-violet rays could only act on the surface layers of living tissue cells.

Animals could also be killed by intensive doses of X-rays and radium. When looking at the pathological picture of animals which had been killed by any form of radiation, one was struck by a common similarity of all of them. He was studying the action of intensive luminous rays and the appearance of animals killed by

ultra-violet rays. He found that the animals often died two or three days after irradiation and showed an area of necrosis in the skin and intestines, with a hæmorrhagic condition of the lung, and what he took to be thrombosis of the coronary vessels of the heart. If the post-mortem examination was carried out immediately after death it would be concluded that the animal died from thrombosis in some of the large vessels.

He had carried out a research with radium, using beta- and gamma-rays. He used small rats weighing 50 gm., and applied a 100-mgm. plaque screened with 1 mm. of silver, and the rat died within four days if about 15 hours' irradiation was given. It was therefore possible to standardize a lethal dose of radium for the rat. Again, as with intensive luminous ultra-violet irradiation, there were areas of necrosis and hæmorrhages in the gut, and there was probably thrombosis in the large vessels.

The hypothesis he wished to put forward, as a consequence, was that these forms of irradiation, by destroying cells, liberated some toxin—a cyto-toxin—which might damage the lining of the blood capillaries and so give rise to death in consequence of a clotting in the large vessels. It was a condition which he would call "radio-toxæmia."

Professor G. H. Wooldridge (President, Section of Comparative Medicine) said that the subject was divisible into two different sections: (1) the use of X-rays for purposes of diagnosis; (2) the curative effects of X-rays and other emanations or forms of light. The greatest sphere so far was the diagnostic, but he agreed with Dr. Salmond that X-rays should not be expected to supplant the ordinary manual examination; they must be looked upon as supplementary, in difficult cases. His own experience had not been with taking radiographs, but with their interpretation, of which he had done a great deal. In many cases he had been unable to get any assistance from X-rays, and sometimes a well-taken skiagram was misleading. He therefore relied chiefly on ordinary clinical methods, though admittedly the rays constituted a valuable supplement.

Major Pryer spoke of the difficulties of radiographing the horse, and it could easily be seen that these difficulties were mostly due to the quantity and density of the body-tissues to be penetrated. It was an easier matter in the case of the feet and the limbs. The technique suggested for radiographing these was doubtless valuable, and he hoped Major Pryer would persevere with it. He, the speaker, recently had to have a horse's foot examined by X-rays to see whether there was any disease of the navicular bone. It would be evident, from the pictures shown during this discussion, that it was not easy to trace simple erosion when superimposed upon a dense layer of bone, perhaps $1\frac{1}{2}$ in. thick. Major Pryer had stated that the presence of spurs at the end of the navicular bone was diagnostic of navicular disease, but in many cases of navicular disease there were no spurs.

His own chief difficulties had been in connection with urinary calculi in the kidney of the dog. So small were these stones and the tissues to be penetrated so dense, that it was very difficult to make them out. Stones in the bladder were easily detected. It was common to find urethral calculi in the male dog $\frac{1}{8}$ in. in diameter; they were arrested at the os penis, just where a tubercle occurred on it. Only by careful and repeated exposure to the rays could these be detected. If the exposure was negative in this situation, he disregarded it and resorted to surgical measures, with good results to the patient.

Some of the skiagrams shown—such as those of cysticerci—were of no service to the clinician. They were from dead specimens, and he suggested that no one would dream of expecting to diagnose by X-rays calcified cysts in the musculature of a domesticated animal. It might not be the same with sarcosporidiosis, because often

these were present without symptoms. In this disease in the sheep and pig X-rays might be useful for detecting it, but one would not imagine the owner of a pig ready to bear the expense of the rays for such a diagnosis; his line would be a matter of economy—if it was fit for food, well and good, if not, it must be destroyed.

With regard to sterilization by X-rays, the subject was interesting, but the surgical process in animals was comparatively easy, and patients did very well after it. Even after excision of ovaries and uterus, the animal would run about in apparent health within a week, and mares had been known to hunt on the day the ovaries had been removed.

His colleague, Professor McCunn, had said he had not been able to see the fœtuses in bitches by X-rays. He, the speaker, had had two successes in that way. A bitch was submitted to him which he had known to have calculus in the bladder. She was then pregnant and had gone a week beyond the normal time for delivery, and the question was as to whether operation should be performed. As she was becoming weak, he decided upon radical operation. The uterus, containing one pup and a portion of another, was removed, and a stone was taken from the bladder at the same time. In that case the puppy and all the details came out clearly in the skiagram.

The use of X-rays in experimental work would do away with the need of much vivisection; many functions, such as swallowing and peristaltic action, could be shown more clearly by X-rays. Shortly this radiograph would be linked up with the cinematograph, and by this means much experimental work in demonstrating physiology would be obviated.

Members of the Section of Comparative Medicine felt that they had yet a long way to go, and not much would be accomplished until a number of veterinarians could afford the time to take up radiology more thoroughly than had been possible up to the present.

Dr. Chalmers Watson said that this discussion had ranged around the word "comparison" and that could be applied in three important directions: (1) in regard to pathological appearances, (2) from the point of view of treatment, (3) from the wider and more important aspect of nutrition. He had hoped to learn from this discussion more of the fundamental aspect of the whole question in regard to nutrition in animal and plant life; all chronic inflammatory and degenerative changes in animals and man were end-results of some definite disturbance of nutrition. If it was true, as Dr. Barclay had stated, that radiology had profoundly modified physiology and clinical medicine, it was still more true to say that the wider application of what was now termed physiotherapy, to the problems of nutrition, to their disturbances in man and animals, and to their treatment, would exercise a much more drastic change in our present teaching and practice.

During the past year he had been directing some attention to diseases in pigs and poultry. Not long ago he had the joints of young pigs examined radiologically, and interesting appearances were seen in the bones and general skeleton. His difficulty, owing to the newness of the subject, was in getting assistance in interpretation from veterinary experts, but, judging from the enthusiasm shown in this discussion, it would probably not be long before that difficulty would be overcome. He had recently spent an interesting afternoon at an experimental poultry farm conducted by the National Poultry Breeders' Association, under a capable head. In one experiment which he had seen, Mr. Newman had tried out results with a much vaunted mash for poultry. That dietary had caused in many animals a complete picture of what is commonly regarded as rickets—a disturbance of nutrition revealed by the state of the feathers, anæmia revealed by physical and mental apathy of the bird, the colour, etc., of the comb, the enlargement of certain joints, and by other deformities. When asked what were the X-ray appearances, Mr. Newman stated that these were

not known. Dr. Fulton, of the radiological department of Edinburgh Royal Infirmary, made a radiological examination of some of these birds, with an interesting result which it was unnecessary to give in detail at the moment.

Nutrition was profoundly important, and should be more carefully studied. The leading commercial houses which produced animal foods for use in the agricultural industry were now advertising irradiated foodstuffs, and it was very important that the commercial exploitation of these foods should not be in excess of what was known. For the past year or two he had been giving attention to ultra-violet rays as applied to milk, applying those rays to whole milk and to milk from which the fat content had been largely removed.

He would suggest that at some subsequent meeting this subject might be again reviewed, taking the wider standpoint of nutrition. Under present conditions the medical members of the Public Health service were specially interested and sympathetic to the subject of "radiation" in all its important bearings.

Section of Tropical Diseases and Parasitology.

[*January* 6, 1931.]

Filariasis in the Dutch East Indies

By S. L. Brug.

(*Geneeskundig Laboratorium, Batavia.*)

(1) *Two species of human filaria in East Asia.*—In 1908 Sambon discussing a paper by Low read in this Society and published in the *Journal of Tropical Medicine and Hygiene*, "believed that under that name" (*Filaria bancrofti*) "several worms had been confounded." I think at present it has been proved that at least two species of filaria have been confounded formerly under the entity "*Filaria bancrofti*."

In Dutch East India the common opinion that *Culex fatigans* is the principal carrier of *F. bancrofti* did not seem to hold good. This mosquito is by preference an urban mosquito; filarial infection in that part of the world is mostly a rural infection, elephantiasis a rural disease. In the Malay Archipelago the distribution of the mosquito on one hand, and of the worm on the other hand, seemed to indicate that filariasis was not generally carried by *C. fatigans*. These considerations induced Lichtenstein (1927), then working in Bireuen (Atchin, Sumatra), to investigate the question of the vector of *F. bancrofti* in his district. His research gave no positive result, but a very important negative one. The Bireuen microfilaria did *not* develop in *C. fatigans*. Lichtenstein used about 300 mosquitoes, the great majority of them belonging to this species; but he could not trace in them a single sausage-shaped stage. He then sent me some slides with blood of the patients on whom the mosquitoes had fed, and requested me to inform him whether microfilaria bancrofti was present in the slides. After ample consideration I concluded that in the slides there was no mf. bancrofti, but microfilariæ of an undescribed species, to which I gave the specific name *malayi*. The question of the designation of the genus has been discussed by Fülleborn (1929), and time does not permit of further discussion here.

Microfilaria malayi.—I described the morphological characters of this new microfilaria in a paper read during the Congress of the Far Eastern Association of Tropical Medicine in Calcutta in 1927. I will not repeat them here in detail, but only call your attention to some differences between mf. malayi and mf. bancrofti which may serve to distinguish them in routine work in slides stained with hæmatoxylin. (In Giemsa- or Leishman- or Kiewiet de Jonge-stained slides the differentiation is much more difficult and often impossible). As may be seen from fig. 1: (*a*) The nuclei of mf. bancrofti are arranged neatly and they may be counted easily; those of mf. malayi are more clotted together, and very careful focusing is necessary in order to count them. (*b*) The anal pore can be distinguished easily in almost any specimen of mf. malayi as an oval unstained spot, situated at about a fifth of the animal's length, measured from the posterior end of the body. In mf. bancrofti (at least in slides stained in the ordinary way with hæmatoxylin) this organ can hardly be detected, and often not at all. (*c*) The tail of mf. bancrofti is quite devoid of nuclei, that of mf. malayi shows two (or sometimes one or three) scattered nuclei, one of which is situated just at its end. These differences will enable one to differentiate almost all the specimens seen. For more detailed information I must refer the reader to my paper read during the Calcutta Congress.

(2) *The geographical distribution.*—The geographical distribution (as far as known) of the two species in Dutch East India shows that there is no sharp line of demarcation. On the map, circles denote the findings of mf. malayi, triangles

those of mf. bancrofti, and crosses those of unidentified microfilariæ. Large marks show an endemic infestation of more than 10% of the adults, small marks an infestation of less than 10%, or the fact that only sporadic cases have been found.

Both the species occur throughout the Archipelago. In Java, Sumatra, Borneo, Celebes, Flores and Soemba both are found; in New Guinea *F. bancrofti* only. Generally mf. malayi is found more frequently. In Java, however, where filariasis is relatively rare, *bancrofti* seems to be the predominant species. In Kabaena, a

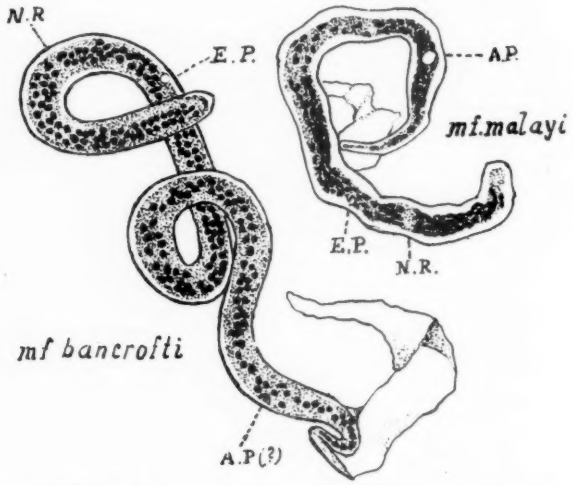


FIG. 1.—Microfilaria bancrofti and microfilaria malayi from human blood.

Findings of microfilaria in the Malay Archipelago.

small island near Celebes, many *bancrofti* were found and no *malayi*. There are a few observations that seem to indicate that the occurrence of *F. malayi* is limited to the plains and that *F. bancrofti* may spread into the hills; however, the number of observations is as yet too small to warrant a more precise opinion on this matter.

(3) *The occurrence of mixed infections of F. bancrofti and F. malayi.*—In villages where both the species of human filaria occur, a curious phenomenon was observed in relation to the mixed infections. Table I proves that in almost all such villages there occur more mixed infections than might be expected in accordance

with the laws of probability, e.g.: in Moekoe Saki out of 115 persons 51 were infected with *F. bancrofti* and five with *F. malayi*. All the five *malayi* coincide with the *bancrofti* cases, not one of them occurs amongst the 64 people free from *bancrofti*.

TABLE I.

Locality	Number of persons examined	Malayi only	Bancrofti only	Mixed infections: Observed	Mixed infections: To be expected (b + d) (c + d)
	(a)	(b)	(c)	(d)	(a)
Semboro (Mamoedjoe) ...	90	15	2	8	$2\frac{1}{2}$
Orabatoe ,, ...	48	6	2	0	$\frac{1}{4}$
Djenparing (Borneo) ...	21	3	5	4	3
Sigli (Atchin)	87	5	11	0	$\frac{2}{3}$
Seulimeun (Atchin) ...	26	2	1	0	$\frac{1}{13}$
Kotta Radja (Atchin) ...	83	3	4	0	$\frac{1}{7}$
Leumpotong Rajoet (Atchin)	61	6	1	1	$\frac{1}{4}$
Soemba	70	5	5	2	$\frac{5}{7}$
Wakoe Seko (Flores) ...	160	19	3	7	$1\frac{5}{8}$
Moekoe Saki (Flores) ...	115	0	46	5	$2\frac{1}{6}$
Maoe Role (Flores) ...	90	5	9	10	3
Sarolangoen (Djambi) ...	146	7	6	5	1
Maoe Tinda (Flores) ...	109	14	2	4	1

My first thought on discovering this phenomenon was that mf. malayi was not the embryo of a new species at all, but a hitherto unknown stage in the life cycle of *F. bancrofti*. However, reflecting over the question, I deemed this hypothesis untenable. In many regions of Dutch East India one of the stages, either the *malayi* or the *bancrofti* "stage," is missing altogether, whereas the other occurs abundantly. If mf. malayi is really only a stage of *F. bancrofti* it would have been discovered long ago by those workers who have closely studied the morphology of mf. bancrofti, especially those who have measured the larvæ. They have paid special attention to the larval tail and could hardly have overlooked the scattered nuclei in it. They all agree that the tail of mf. bancrofti is devoid of nuclei. In their cases apparently the *malayi* "stage" was wholly absent.

I have tried to explain the phenomenon by another hypothesis, viz., the existence of a greater or lesser immunity to both species in the same individual or a certain predisposition to infection with both species in one person.

(4) *The carriers of F. malayi.*—An investigation of the carriers of *F. malayi* has been made by De Rook and Brug (1930). It was made in the Benkulen region of Sumatra in two small villages near the coast. In the villages 47% of the population (children included) harboured *F. malayi* embryos, and amongst 225 persons we could not detect a single case of *bancrofti*-infection. We caught some thousands of mosquitoes in human habitations; amongst them there was not a single specimen of *Culex fatigans*. So we were unable to confirm experimentally Lichtenstein's finding that mf. malayi does not develop in this mosquito, but its absence in a focus so heavily infected with this worm seems to be in favour of his conclusions.

Artificial, as well as natural, infection of the mosquitoes was studied. In order to investigate the former, we caught, during the evening, all the mosquitoes that had fed on a heavily infected person. As soon as a mosquito had inserted its proboscis in the skin of the patient, a test tube was carefully put over it and held in position until the gnat was gorged and flew into the test tube. In this way about five "catchers" were occupied with one patient. During a "good" evening some hundred gorged mosquitoes could be caught. In order to keep them living, a maximal degree of humidity proved to be the most important condition. There was always a great mortality amongst our mosquitoes, but usually more than 10% survived 10 to 15 days, long enough to show the complete development of the ingested microfilariæ. The results of investigating the artificial infections are shown in

Table II. This shows that in the villages we investigated, *Tæniorhynchus* (*Mansonioides*) *annulatus* and *T.* (*M.*) *annulipes* were by far the most common man-biting mosquitoes, and that the survival of microfilaria practically occurred only in these two species and in two other species belonging to the same subgenus, viz., *T.* (*M.*) *uniformis* and *T.* (*M.*) *annuliferus*: these two, however, were far less abundant.

TABLE II.

Days in mosquito	Tæniorhynchus: Mansonioides: annulipes		annulatus		uniformis		annuliferus		Coquillettidia giblini		Culex spp.		Aëdes spp.		Anopheles spp.	
	+	−	+	−	+	−	+	−	+	−	+	−	+	−	+	−
½	6	...	8	1	1	...	...	...	1	...	1	...	...	...	...	1
1½	6	...	18	5	1	...	...	...	...	...	...	2	...	...	...	...
2½	4	4	18	3	...	...	...	...	2	1	1	3	...	2	...	...
3½	3	1	29	4	...	...	...	...	...	...	...	11	..	1	...	...
4½	5	...	6	1	1	...	...	...	...	1	...	9	...	2	...	1
5½	2	...	9	2	1	...	...	...	...	...	...	9	1	...	..	...
6½	7	2	10	5	2	...	...	...	...	1	...	1	...	...	...	...
7½	17	...	7	5	...	...	...	...	...	2	...	3	...	..	...	...
8½	8	1	15	...	1	..	1	...	...	1	...	...	...	1	...	...
9½	13	...	9	2	...	...	...	...	...	...	...	...	...	..	...	...
10½	6	...	7	...	...	...	...	...	...	1	...	1	...	...	...	...
11½	5	...	6	...	...	...	...	...	...	1	...	2	...	...	...	...
12½	6	...	2	2	...	..	...	...	...	...	...	...	...	...	...	...
13½	5	...	2	...	...	...	...	...	...	...	...	...	...	...	...	...
14½	2	...	1	...	...	...	...	...	...	...	...	...	...	...	...	...
15½	2	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
16½	2	...	1	...	...	...	...	...	...	...	...	...	...	...	...	...
17½	2	...	...	...	...	..	...	..	...	...	...	...	...	...	...	...
—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Total	101	8	148	30	7	0	1	0	3	8	2	41	1	6	0	2
	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Per cent.	93	7	83	17	...	...	...	...	...	...	...	...	...	...	...	...

The *Culex* were:
C. tritæniorhynchus (2 positive) 30
C. gelidus 7
C. vishnui 1
C. whitmorei 4
C. bitæniorhynchus 1

The *Aëdes* were:
A. (*Ædimorphus*) *vexans* ... 5
A. (*Finlaya*) *poicilia* 1
A. (*Aëdes*) sp. (positive) ... 1

The *Anopheles* were:
A. kochi 1
A. tesselatus 1

It is curious that in *Tæniorhynchus* (*Coquillettidia*) *giblini*, belonging to the same genus but to another subgenus, the microfilaria did not live more than two and a half days.

The following diagram (p. 27) gives the length of the microfilariæ found in mosquitoes in which they survived. Each horizontal line represents one mosquito, and each dot the length of one larva. The length of microfilaria as found in the human blood is about 250μ. It is clear that the growth in length begins at about the sixth day, and that at about the eleventh day the maximal length of some 1·5 mm. is reached. Further, the diagram shows that even in the same mosquito the various microfilariæ have a very great range of growth. Fig. 2 shows in a more popular, but less, exact way the initial decrease in size and the subsequent growth of the microfilariæ from the sixth to the twelfth day,

Figs. 3 and 4 (1 to 17) show the structure of the larvæ as seen in dissected mosquitoes. We had no opportunity to compare the morphology of the stages of development of mf. malayi in mosquitoes with that of mf. bancrofti. In general the development of mf. malayi is very similar to that of mf. bancrofti as described in textbooks. I call your attention to two features that may be particular for mf. malayi: (1) During the "sausage" stage, which lasts about five days, the tail with the scattered nuclei usually is preserved. This fact clearly indicates that the forms as seen were indeed stages of mf. malayi. (2) In larvæ that have

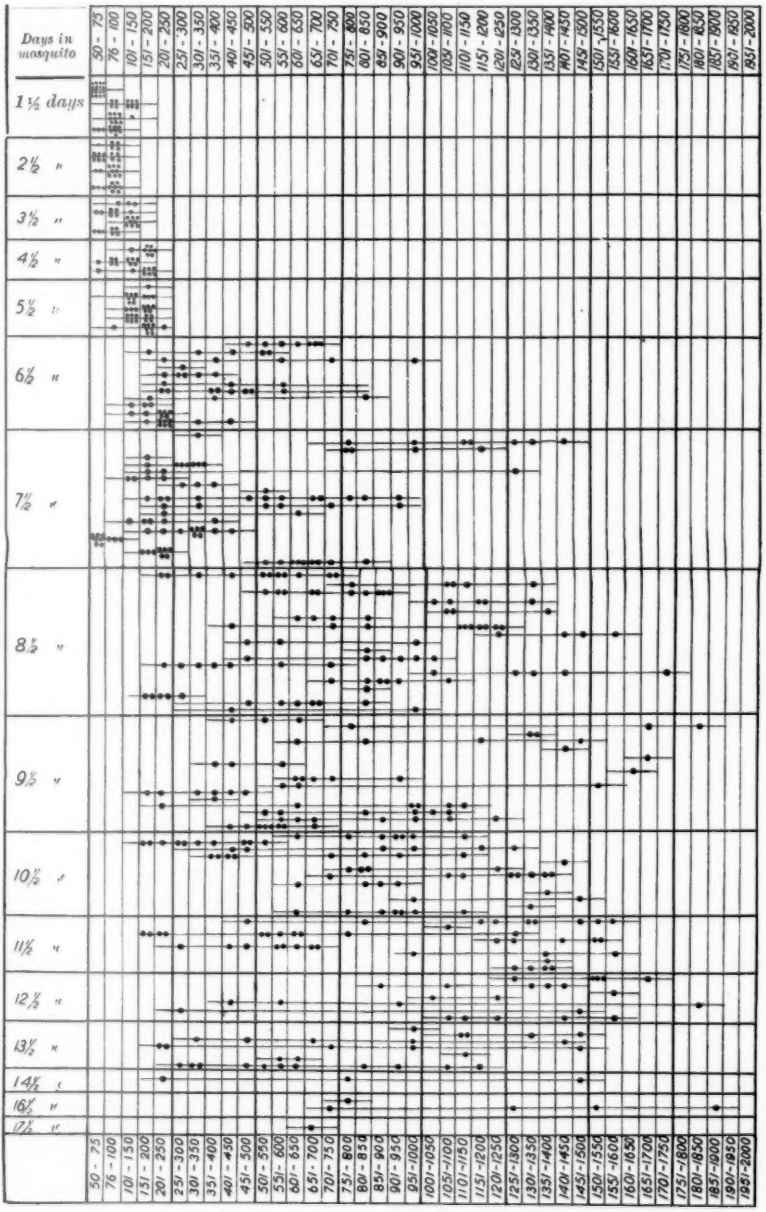


Diagram showing length of *Filaria malayi* in *Tæniorhynchus* (*Mansonioides*) *annulipes* and *T.* (*M.*) *annulatus*.

stayed for about 7 to 10 days in the insect, a particular structure is often seen in the anus. It has the form of a nail with its head outside the anus and its pin in the hind gut. It stains darkly with hæmatoxylin and shows no cellular structure. As far as I know nothing analogous to it has ever been described in *bancrofti* larvæ. I have not the faintest idea what it is.

The investigation of the natural infection of mosquitoes caught in houses was necessary as a control of the artificial infection, or, in other words, to make sure that our artificial infection really was the result of a blood meal from an infected human being. We found that practically only the two above mentioned, abundantly occurring *Mansonioides* species (*annulipes* and *annulatus*) were naturally infected

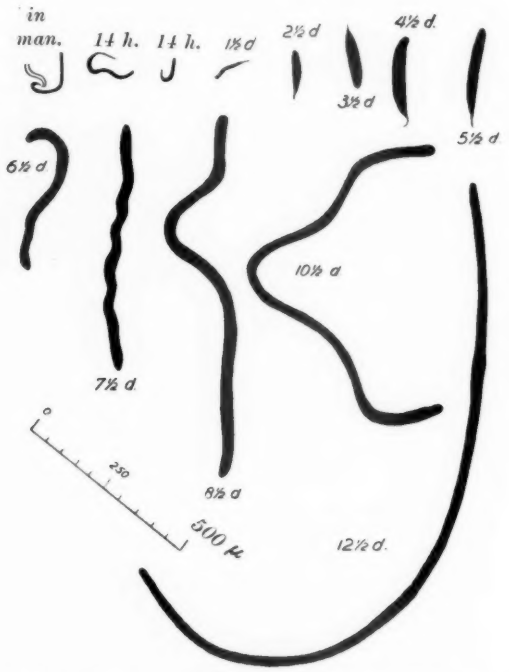


FIG. 2.—Schematic representation of growth of mf. malayi in mosquito.

(Table III). Most of the naturally infected mosquitoes showed a fairly advanced stage of infection. This may be attributed to the time between the infective repast and the next visit to a human habitation. The percentage of naturally infected mosquitoes was very low; we had expected to find a higher percentage. There is a discordance between the large number of infected human beings and the small number of naturally infected mosquitoes. We experienced personally that the species we dealt with were very anthropophagous. I think there must be a very great loss of mosquitoes between the infective feed and the next visit to a human dwelling.

TABLE III.

Natural infection	No. dissected	Positive	
		No.	Percentage
Tæniorhynchus (Mansonioides) annulatus	323	6	1·9%
" " *annulipes*	339	4	1·2%
" " *uniformis*	7	0	—
Culex, spp.	13	0	—
Aëdes, spp.	16	0	—
Anopheles, spp.	5	0	—

The natural infection index, however small, is great enough to explain the heavy infestation of the population. On a good mosquito evening we were bitten by about

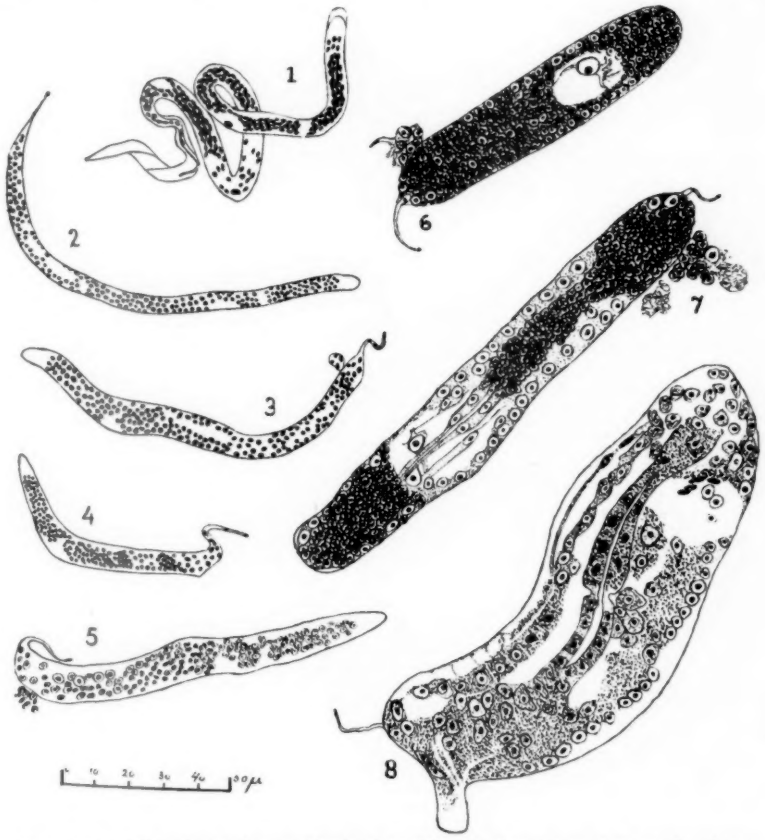


FIG. 3.—1. Mf. malayi in human blood. 2-8.—Mf. malayi in thorax of *Tæniorhynchus (Mansonioides) annulipes* and *T. (M.) annulatus*, ½-4½ day.

a hundred mosquitoes before eleven o'clock, and then they drove us to bed; the number of assailants increased very much after ten o'clock. The prevalence of the carrying mosquitoes is great enough to explain why half the population was infected. It would be far more difficult to explain why the other half was not.

I must now state that in mosquitoes with artificial infection, as well as in those with natural infection, we found specimens with proboscis infection. In the artificially infected ones the larvæ were found in the proboscis after about eleven days and later.

To be brief, we found that very probably *Mansonioides* species play an important rôle as vectors of mf. malayi. It will be difficult, experimentally, to prove that the mosquitoes with proboscis infection can infect man. Even for *F. bancrofti* this experiment has not yet been made.

As regards the carrying of *F. bancrofti* I only want to call attention to the fact that in New Guinea this worm frequently occurs in the absence of *C. fatigans*, just as in the New Hebrides (Buxton and Hopkins, 1927). Further, that Daniels found development of mf. bancrofti in *Mansonioides* species in Africa, and Leicester (1908) in Malaya; and Manson-Bahr (1912) notes that in Ceylon the distribution of *Mansonioides* is more in accordance with the occurrence of filariasis than that of *C. fatigans*. Manson-Bahr expressly states that the microfilariæ in Ceylon are not different from those of *F. bancrofti* from other regions.

I regret I cannot give you many particulars regarding the biology of the *Mansonioides* species with which we dealt. They are fierce man-biters. The bite may be felt as a sting, unlike that of, e.g., *Stegomyia fasciata*. The subsequent itching is moderate, at least for a tropical "old hand." These mosquitoes enter human dwellings at about 7 o'clock in the evening. Their attacks begin at about 8 o'clock and become unbearable at 10 o'clock. They enter the house by preference when it rains; even heavy rain does not check them. We could not explain how they managed to fly through the rain. After sunny days there were few mosquitoes. This is quite different from our experience in Batavia, where a rainy afternoon means a mosquito-free evening.

In spite of the tremendous number of *Mansonioides* imagos, a fourteen days' search failed to reveal us a single breeding place; Senior White (1927) had the same experience with *T. (M.) uniformis* in Ceylon. There was a large swamp near our village with virgin forest within it. In this forest we could find very many adult *Mansonioides* throughout the day, but no larvæ were detected. We failed also to obtain adults with mosquito nets suspended on the water.

(5) *The periodicity of mf. malayi.*—Mf. malayi shows a nocturnal periodicity. During the night the number of microfilariæ in the peripheral blood is always much larger than at noon. The nocturnal periodicity of mf. malayi is less absolute than of mf. bancrofti. The relation:

$$\frac{\text{number of mf. at noon}}{\text{number of mf. at night}}$$

has been proved to be more than 1/50 (mean 1/15-1/20) in *malayi* and less than 1/100 in *bancrofti* (Van Slee, 1930; De Rook, 1930). Buxton and Hopkins (1927) found this relation in the New Hebrides about 1/50 for *bancrofti*. In a well-studied case the curve of the number of mf. malayi in the peripheral blood showed two apices during the night, one at 8 o'clock and one at 4 o'clock, with a depression at midnight. In a fisherman at Mamoedjoe (Celebes) who worked during the night and slept in the daytime, Van Slee (1930) found a diurnal periodicity.

(6) *The symptomatology of filariasis.*—The question arises: "Is *F. malayi* pathogenic? Can it produce the same symptoms as *F. bancrofti* (or others)?" In the first place the relation between *F. malayi* and elephantiasis must be discussed. This relation can best be studied in regions where this worm occurs frequently and where *F. bancrofti* is wholly absent. Such areas are: the West Coast of Atchin, the coastal area of Benkulen, the Pinrang district and the Northern Mamoedjoe districts in Celebes, and the village Kawata in the same island. In all of them

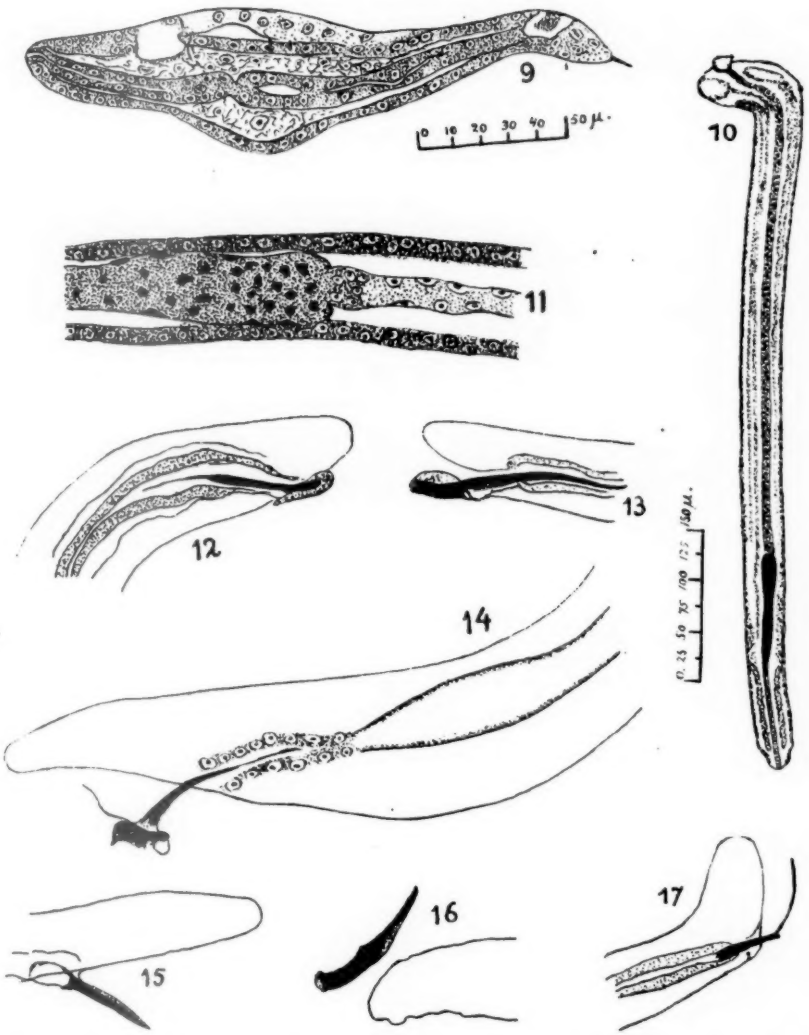


FIG. 4.—Mf. malayi in thorax of *T.* (*M.*) *annulipes* and *T.* (*M.*) *annulatus*. 9-10.—5½ and 6½ day in mosquito. 11.—Transition from œsophagus to midgut. 12-14.—" Anal Nail " 15-17—Ejection (♂) of anal nail.

elephantiasis of the limbs (especially of the legs) has been found frequently. Only the coastal area of Benkulen is an exception, elephantiasis being almost wholly absent there. The most interesting observations have been made in Celebes; in Mamoedjoe by Van Slee (1930) and in Kawata by Gothein (not published). Their observations may be summarized in this table:—

TABLE IV.

	No. examined	No. harbouring Mf. malayi	Infection index	
Northern part of Mamoedjoe:				
Adults chosen at random ...	802	220	27% ± 1·6%	difference
Elephantiasis patients ...	26*	20	77% ± 8·3%	50% ± 8·4%
Kawata:				
Adults chosen at random ...	118	33	28% ± 4·1%	difference
Elephantiasis patients ...	10	8	80% ± 12·7%	52% ± 13·3%

* Moreover, 58 elephantiasis patients were seen whose blood was not examined at night.

This not only shows the prevalence of elephantiasis in regions strongly infested with *F. malayi* and free from *F. bancrofti*, but also proves the existence of a close association between the disease and the infestation with the worms. In both areas the infection index of the diseased people is much higher than that of the population as a whole; the differences are statistically important. This phenomenon is just the reverse of that observed in most of the *bancrofti* areas where similar investigations have been made; in these regions the infection index of the elephantiasis patients was generally less than that of the population in general.

Other symptoms that might be ascribed to filarial infection were rarely seen in pure *malayi* areas, and further observation is needed to solve the question whether *F. malayi* can produce them.

Areas wholly or mainly infested with *F. bancrofti* have been discovered in Kabaena, a small island south of Celebes, by Reeling Knap (1930) and in New Guinea by De Rook (1930) and Leimena (not published). In Kabaena, Reeling Knap found endemic hydrocele prevalent amongst the population, who showed a *bancrofti* index of 29%, whereas no mf. malayi was found there; elephantiasis was wholly absent or at least very rare. In New Guinea, De Rook found enlargement of the scrotum very common amongst the Papuas, a *bancrofti* index of about 25% and no autochthonous cases of mf. malayi infection. Elephantiasis of the limbs also occurred amongst the tribe studied by him, but it was relatively rare. Only five out of some 500 male adults suffered from it.

Thus observations in Dutch East India fully confirm Korke's statement (1929) that the "typical form of mf. bancrofti" seems to be more associated with affections of the genitalia, and the "atypical form" more with elephantiasis of the limbs. The atypical form of mf. malayi of Korke is the same as my mf. malayi.

In this paper I have tried to give some idea of the filarial problems that now occupy us in the Malay Archipelago. It is only a rapid review, not a complete record of all that has been found hitherto. For more detailed information I would refer you to the Dutch publications that have been issued in the *Geneeskundig Tijdschrift voor Nederlandsch-Indië*.

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Discussion.—Dr. G. CARMICHAEL LOW said that the diagnosis of a new species of *Filaria bancrofti*, from the embryonic form alone, was one fraught with great difficulty. If the morphology was sufficiently distinctive, then it could be made, but an examination of the adults, both as to morphology and the site of the body which they inhabited, was necessary before coming to conclusions about diagnosis. Members of the Section would remember that Professor Leiper had decided, after a careful examination of the adult forms found by Dr. Manson-Bahr in Fiji, that they could not be separated from *F. bancrofti* on morphological grounds, yet here the embryos were non-periodic and developed in a different mosquito from the typical strain. It might be that change of climate had influenced this and there was little doubt that this form was a race or subspecies, if such a thing is recognized in helminthology, of *F. bancrofti*.

Colonel Brug's work showed that the embryo described by him was different in several morphological points from the typical *F. bancrofti* and also would not develop in *Culex fatigans*. It would be interesting if, when he returned to Batavia, he would work out the intermediate host of his new filaria—*Filaria malayi*—and also do some experimental work with other species. It was impossible to say that it could, even if it were a true species, cause elephantiasis until the adults had been found and the exact site which they occupied in the body determined.

The relationship between Craig's *Filaria philippinensis* and Colonel Brug's *Filaria malayi* might be worked out. The former, of course, was said to be non-periodic, a point of distinction between it and the latter. The whole subject of *Filaria bancrofti* required new study, but until more adults were obtained from a different part of the world, this could not be done satisfactorily.

Dr. MANSON-BAHR said he considered that Colonel Brug's paper was undoubtedly the most important contribution to the subject of filariasis for the last fifteen years. From the morphology of the embryo filaria and its development in a particular mosquito—*Mansonioides*—it was undoubtedly a distinct entity. Its relationship to elephantiasis was also striking, and he wondered how much reliance could be placed upon minor differences in clinical pathology as indicating specific differences in the parasites. He had re-examined his Fiji and Ceylon blood-slides of filaria to see whether he had by chance missed the characteristic tail nuclei of *malayi*, but he had not. It would be necessary in the light of these discoveries to re-study the conditions in Ceylon as he (the speaker) had noted the prevalence of *Mansonioides* in association with filariasis in that island. Filariasis was a fascinating subject and he wondered what might be the relation of *malayi* to the non-periodic Pacific filaria and what the correct nomenclature of the latter should be. In helminthology it was too commonly assumed that similar morphology stipulated identical species, but this was not necessarily the case. It was possible that the Pacific non-periodic filaria adult was distinct in many senses from the original *Filaria bancrofti* of India and the Far East.

Dr. GEORGE W. BRAY: In 1926 I had the opportunity of determining the incidence of microfilaria in the blood of the native population of Nauru (Central Pacific). With the exception of infants the entire native population numbering 1,151 Nauruans was examined. The technique adopted was to take a drop of blood from the prick of a finger or ear, place it on a clean slide, cover it with a coverslip, and examine it at once. Only one examination was made in each case. Microfilariæ were found in 332 cases, or 28·8% of the population, 195 (58·7%) being males and 137 (41·3%) females. The microfilariæ had a definite nocturnal periodicity.

Elephantiasis was comparatively rare; four males and two females had a mild condition of one leg, whilst in one boy, aged 16, the affection was gross. In six males the scrotum was involved and in two women the breast; in all cases the affection was mild. Repeated examinations failed to demonstrate microfilariæ in the blood of these patients.

High fevers, lymphangiitis, adenitis and abscess formation were extremely frequent. Ten per cent. of the male population had small chronic hydroceles.

Colonel CLAYTON LANE said that there was need for examination of adult forms in attempting to determine whether mf. malayi represented a good species. Korke had reported that a microfilaria which he had found in Orissa, India, resembled mf. malayi, and Colonel Brug held that it was mf. malayi, in which case that form was more widely spread than was at present suspected.

Section of Dermatology.

[*January* 15, 1931.]

? Trichokyptomania: Case for Diagnosis.—H. MACCORMAC, C.B.E., M.D., and H. W. BARBER, M.B.

A. W., aged 13. The patient has had good health and an exceptionally fine head of hair. On June 6, 1930, her parents visited her at school at Brighton, and noticed that the hair had receded from the temples, in front, and on the right side behind the ear, but these areas were covered with short "bristly" hair. Two weeks previously there had been nothing noticeably wrong with the hair. She was brought back to London, and saw Dr. Muende, and the hair grew again satisfactorily.

In the first week in November, the parents again noticed that the hair on the vertex began to get thin, as well as in front and over the temples. She was seen by us separately, and later together in consultation.

On the vertex of the scalp, the frontal regions and the temples the hair is broken off and numerous short stumps are seen. Examination with a lens reveals some hyperkeratosis of the follicles, such as are seen in keratosis pilaris. The pubic hair is affected, there being follicular keratosis with some pustules. Microscopical examination of the stumps does not show the characteristic beading of monilethrix, nor are the appearances quite those of trichorrhexis nodosa, although some hairs exhibit a modified form of "green-stick fracture."

At first we both considered the possibility of trichokyptomania, but the hyperkeratosis at the mouths of the hair follicles on the scalp and pubis is difficult to explain on this assumption.

Discussion.—Dr. W. J. O'DONOVAN said that the patient had a heavy, sullen, self-conscious, almost a "guilty" look. She was suspicious of questions, and, when approached, flushed, stiffened, breathed heavily and seemed unconscious. This quasi-hysterical attack came on when the conjunctiva was touched. The mother's description of the sudden appearance of bald patches covered by short bristles led him (the speaker) to adhere to the exhibitors' first suggestion. The history, too, that this condition came on, completely cleared away, and then recurred suddenly, seemed to him conclusive evidence that the case as a whole was a neurosis of the type called trichorrhexomania.

Dr. A. C. ROXBURGH agreed with Dr. O'Donovan; he thought the girl produced the condition herself, either by tugging the hair or rubbing it, perhaps by using a safety-razor on it.

The PRESIDENT said he thought the presence of keratosis of the hair follicles was in favour of a diagnosis of monilethrix, as he had never seen this condition associated with trichotillomania; otherwise he thought there was nothing against the latter diagnosis in the present case.

Dr. SEMON said he thought the diagnosis might be settled by a neurologist.

Sclerema Neonatorum.—J. E. M. WIGLEY, M.B.

On December 31, 1930, a male infant, aged 4 weeks, was admitted to the Children's Hospital, Paddington Green. The mother said that there was a "lump on his back."

He had been born at full time, and the labour was natural; he was blue at birth, and was revived by artificial means. During the first two days of life he suffered from fits of a mild nature. When he was one week old, the mother had observed

the swelling on the back; during the second week this increased in size, and other swellings appeared on the left shoulder and left thigh. The skin covering these areas was reddened.

On examination he was seen to be well nourished and apparently healthy. The skin was affected in three situations. There were (1) a large, roughly circular, area on the back of the thorax, some 3 in. in diameter, (2) a smaller area over the left shoulder, and arm extending as far down as the middle of the forearm, (3) a third, still smaller, patch on the outer surface of the left thigh. These areas of skin were purplish in colour and indurated. The edges were easily defined by palpation, had an irregular outline, and corresponded with the limits of the discoloration. The skin could not be pinched up, but the whole mass was freely movable on the deeper structures. The area over the left shoulder was apparently tender on pressure. In no situation was there any evidence of cyst formation. The liver edge was palpable $\frac{3}{4}$ in. below the costal margin.

Since admission to hospital, the child's condition has altered but little. Diarrhœa with green stools has been intermittent throughout. There has been no loss of weight.

The deep purple colour of the lesions has gradually faded, leaving now only a pink discoloration of the skin. The margins of the lesions are less easily defined by palpation than at the time of admission to hospital. This applies in particular to the lower border of the area on the back.

Temperature has varied between 97·6° and 100·8° F. Wassermann reaction is negative.

Radiographic examinations revealed the presence of an L-shaped opacity in the left ante-cubital fossa.

This case corresponds with those previously reported by Dr. Harrison in the *Archives of Diseases of Childhood*, of 1926, and by Dr. Konstam, in the same Journal in 1927. Dr. Konstam kindly saw this case for me, and identified it with the case reported by himself. The prognosis is apparently not favourable, as in five out of the six cases reported by these authors the children died. In several of the cases radiographic examination showed numerous granular shadows in the superficial tissues.

Chemical examination of the fat reported by the above authors showed it to be "probably a neutral fat," showing no hydrolysis or saponification.

Discussion.—Dr. F. PARKES WEBER asked whether in other similar cases there had been radiological evidence of any calcareous deposit, as there was in the present case; he took it that these shadows represented commencing calcareous deposits in the affected areas. Calcareous deposition in human pathology was more usually associated with the deposition of lipoids than of neutral fat. He agreed with the diagnosis.

? Lupus Erythematosus of the Buccal Mucous Membrane (previously shown).[1]—H. W. BARBER, M.B.

J. G., aged 41, married. This patient was previously shown by me at a meeting of the Section in November, 1929, and before the British Association of Dermatology in July, 1930. I am showing her again in order to demonstrate the slow but steady improvement that has taken place. In November, 1929, the condition of the buccal mucous membrane had been present for some two years. At that time the dorsal and lateral surfaces of the tongue were covered with irregular white patches; there was also definite inflammatory reddening, with a certain degree of atrophy, and a superficial ulcer on the left side. The mucous membranes of both cheeks were affected, there being white patches on an erythematous base.

[1] *Proceedings*. 1930, xxiii, 353 (Sect. Derm. 9).

I pointed out that the erythematous patches with atrophy were against the diagnosis of lichen planus. At my request Dr. Forman performed :—

(1) The Von Pirquet test, using human and bovine tuberculin ; this was completely negative in all dilutions.

(2) Intradermal tests with emulsions of :—

(*a*) *Streptococcus hæmolyticus* ; strongly positive.

(*b*) *Streptococcus viridans* ; rather less so.

(*c*) Staphylococci ; slightly positive.

(*d*) Normal saline.

There was severe oral sepsis, which has been treated. Injections of solganal were given without evident effect, but since she has had weekly intradermal injections of a streptococcal vaccine, improvement has been progressive. The left cheek is now clear, and the tongue and right cheek have improved considerably.

Lichen Nitidus with Hyperkeratosis of the Palms.—H. W. BARBER, M.B.

H. M., male, aged 48. The history is indefinite. He was first seen by me on December 17, 1930.

Condition.—Palms: Numerous papules with marked hyperkeratosis and a tendency to fissuring. Forearms: Lichenoid papules, mostly follicular, on the anterior surfaces. Characteristic closely-set papules on the extensor surfaces. Legs : Reddish, scaly patches, in which small papules can be distinguished. Popliteal spaces, thighs, and outer surfaces of buttocks are also involved. One hyperkeratotic patch on the inner side of the left heel. Buccal mucous membrane: Whitish plaques on each side of the hard palate and some patches on the left cheek.

Histological report on sections.—Two biopsies were made, one from a forearm and one from a leg. The characteristic cell infiltration with erosion of the epidermis is seen. In the sections from the forearm the follicular localization is well seen.

Extreme Xanthelasma Palpebrarum.—F. PARKES WEBER, M.D.

The patient, Mrs. A. B., aged 63½ years, a Jewish woman born in Poland, has extreme xanthelasma palpebrarum (see figure), which has gradually developed during the last few years, and now involves the whole cutaneous surface of both eyelids of both eyes. The affected skin, of a brownish colour, is considerably elevated. With the exception of some general pruritus (especially of the vulva)

Xanthelasma palpebrarum (Dr. F. Parkes Weber's case).

and certain paræsthetic feelings, she has enjoyed good health, but her brachial blood-pressure is rather high (190/120 mm. Hg) and the heart extends a little too far to the left, and she is now under treatment in the eye department for chronic bilateral glaucoma. No arcus senilis. No xanthoma elsewhere. No cutaneous "xanthosis" (from lipochrome or carotinoid pigmentation) on the hands or feet. No enlargement of liver or spleen. No jaundice and no previous history of any jaundice. The blood-picture and urine show nothing abnormal. There is a faintly positive indirect Hijmans van den Bergh reaction for bilirubin in the blood-serum (practically within normal limits). Blood-sugar: 0·133%. Blood-calcium: 11 mg. % (serum). Blood-cholesterol: 160 mg. % (serum). Negative Wassermann reaction.

In cases like the present one the xanthelasma seems to be due to a local lipoid infiltration connected with local predisposition, which is sometimes familial. In one younger woman I have been able to observe spontaneous disappearance of (very slight) xanthelasma palpebrarum. The carotinoid or lipochrome pigmentation of cutaneous areas infiltrated with cholesterol is interesting when one remembers that carotin and cholesterol are supposed to be fore-stages of vitamins A and D respectively, and that these vitamins are sometimes naturally associated with each other, as in cod-liver oil. It would be interesting to know if the children of xanthelasmic parents are specially free from rickets.

Discussion.—Dr. A. C. ROXBURGH said that Kromayer, in his latest book,[1] advised excision in these cases, and Dr. H. G. Adamson usually adopted that procedure. If the yellow material was shelled out, the skin edges fell together again, without any need for stitches.

The PRESIDENT said that excision would probably be the best form of treatment in this case. The lesions were too much infiltrated for the use of trichloracetic acid, the galvano-cautery, or ultra-violet light.

Dr. KINGSTON BARTON said that the condition appeared to him so local that he asked the patient whether she had spent many years crying and rubbing her eyes, thus causing this hypertrophy, and the daughter spoke up and said: "Yes; that is what she has been doing all her life."

Hodgkin's Disease, with Unusual Eruption.—HENRY MACCORMAC, C.B.E., M.D.

The patient, a man aged 40, was admitted into Middlesex Hospital under the care of Dr. R. A. Young, in September, 1930.

Previous history.—Recent attacks of giddiness and pain in the left side. Since childhood had had an intermittent discharge from the left ear.

On admission.—Complexion was unusually florid. A collar of enlarged glands surrounded the neck, and enlarged glands were observed elsewhere. The spleen was easily felt. An X-ray examination showed heavy root shadows with accentuated striation throughout the lung fields, and some shadowing over the right apex as met with in tuberculosis. The blood-count was as follows: R.B.C.s. 6,420,000; Hb. 114%; W.B.C.s: Polys. 72%; lymphos. 21%; large monos. 3%; eosinos. 3%; mast cells 1%.

There was thus evidence of some degree of polycythæmia, but nothing indicating any phase of leukæmia. One of the enlarged glands removed for microscopic examination showed loss of follicular structure with numerous large lymphocytes suggesting a lymphosarcoma of chronic type. The Wassermann reaction was completely negative.

The clinical picture regarded as a whole resembled either Hodgkin's disease or a chronic lymphosarcoma. The interpretation of the rash is therefore of some importance in relation to the diagnosis. The eruption developed suddenly in November, 1930, after a course of deep X-ray therapy. It is observed principally over the trunk, is profuse, and consists of small erythematous and pigmented patches,

[1] "The Cosmetic Treatment of Skin Complaints," London, 1930.

lichenoid papules and numerous scattered purpuric spots. Although it does not altogether correspond with the better known forms of pseudo-lymphanides, its general aspect, and especially the purpuric elements, suggest a relationship to this group to which, unless it represents an independent condition, it appears to belong.

Discussion.—Dr. H. C. SEMON said that in a paper read by Sir Humphry Rolleston (Fourth Annual Meeting of British Association of Dermatology and Syphilology, *Brit. Journ. Dermat.*, 1924, xxxvi), this peculiar sequela—a pruriginous eruption after exposure to X-rays—had been noted.

Reference to the original quotation (p. 409) elicited the fact that the case was one not of lymphadenoma, but of chronic lymphoid leukæmia, "which after two exposures to X-rays, each of them followed by a rigor, developed in a few hours a widespread papular eruption somewhat resembling measles."

Dr. PARKES WEBER said that he regarded this as a case of erythræmia, i.e., splenomegalic polycythæmia, the enlargement of the spleen being part of the erythræmia. That was suggested especially by the hyperæmic appearance of the mouth and lips. The question arose as to why he had some degree of enlargement of superficial lymphatic glands. There was little evidence in favour of those glands being due to Hodgkin's disease; they had been rather too symmetrical for early Hodgkin's disease. Also in the "biopsy" examination there appeared to have been no Hodgkin's disease giant-cells. He would therefore eliminate Hodgkin's disease. What, then, could this be? He had recently, in collaboration with a colleague, written a paper[1] in which he strongly advocated the view that all cases of erythræmia were allied to myeloid leukæmia. In that article they stated that there was a chain of diseases, erythræmia at one end and typical myeloid leukæmia at the other end, various types of so-called "erythro-leukæmia," though all rare, forming an "erythro-leukæmic chain" between the two. The enlarged glands in the present case might suggest that it was one of an erythro-leukæmic type of erythræmia, though at present the blood-count was not one of myeloid leukæmia. He thought that the eruption was probably the result of X-ray treatment, but that the erythræmia was the predisposing cause.[2]

Dr. STOLKIND said that if there were no eruption in this case he would call it erythræmia vera. He agreed with Dr. Parkes Weber's views. He had under observation three cases, one of which was treated with deep X-rays with the subsequent development of an eruption, which, however, was not quite like that in this case.

Dr. W. J. O'DONOVAN said that though the glands to-day were small, they had been described by the patient as like a collar round the neck, and that suggested Hodgkin's disease. Sometimes Hodgkin's disease began as a large localized lymphadenoid mass, sometimes it had a symmetrical distribution. The glands in this case had disappeared after X-ray therapy, and this frequently occurred in Hodgkin's disease. In erythræmia a notable enlargement of lymphatic glands was a unique phenomenon. An ordinary case of erythræmia would not have only six million red cells.

Dr. MACCORMAC (in reply) said that he thought the microscopical appearance of the glands hardly fitted into the picture that Dr. Parkes Weber had suggested.

Mycosis Fungoides with Papillomatosis of the Areolæ.—M. SYDNEY THOMSON, M.D.

Miss M. A. E. C., aged 39, first noticed some overgrowth of the left areola and nipple about three years ago. The right breast began to show similar changes nine months later. Both caused some irritation and were "rubbed till sore." Sent up with the diagnosis of Paget's eczema, she was first seen by me in May, 1929, when the condition of the breasts was exactly as it is to-day. The papillomatosis of the areola and "cupping" of the nipple is well seen in the accompanying

1 F. P. Weber and O. B. Bode, *Klin. Wochenschrift*, Berlin, 1930, ix, p. 2244. Cf. also F. P. Weber, "The Erythroleukæmic Chain," *Med. Press*, 1929, clxxix, p. 475.

2 With regard to a polycythæmic or erythræmic dermatosis, compare W. Richter, *Dermat. Wochenschrift*, 1925, lxxx, p. 1075.

FIG. 1.

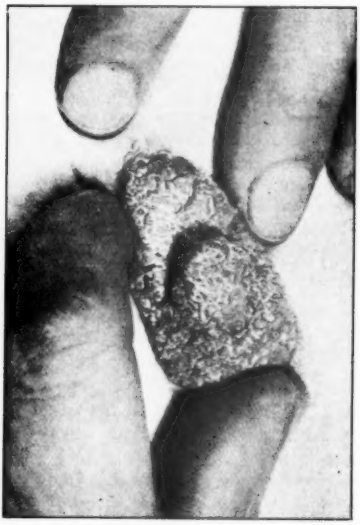


FIG. 2.

illustrations (figs. 1 and 2). At the same time there was observed a very slight and indefinite dermatitis of the legs and arms, this being attributed to the mild xeroderma present. She was admitted to hospital where pathological investigations were made with negative results. She was seen by Sir Lenthal Cheatle and many members of the staff of King's College Hospital. Several possible diagnoses were considered—acanthosis nigricans, pemphigus vegetans, etc.—it finally being decided to treat the case as one of pyogenic papillomatosis. The patient then left hospital, but wrote to

FIG. 3.

say that the condition persisted unaltered. She was not seen again until December, 1930, when she stated that a rash had appeared on the abdomen three months before. The condition then seen is shown in figures 3 and 4, and led to the immediate diagnosis of mycosis fungoides on its general aspect, infiltration, the presence of islands of apparently normal skin, the very marked itching, which was causing insomnia, and the typical red scaly condition of the scalp. Biopsy and the result of the first exposures to X-rays would seem to confirm the diagnosis.

I have been unable to find any reference to this condition of the breasts, but there is an illustration in Sutton's book (p. 666 of the 1919 edition) which suggests

the same tendency to proliferation of the areolæ. Although no biopsy of the breast has yet been made, the early history of this case permits the hypothesis that the local changes are part of the mycosis fungoides.

FIG. 4.

Discussion.—The PRESIDENT said he had seen increased pigmentation and enlargement of the nipples in a case of mycosis fungoides, but he did not ever remember having seen an actual growth affecting the nipple as in the present case.

Dr. W. J. O'DONOVAN said that a fortnight ago he had had an exactly similar case located to one nipple. He had tried an application of radium externally, using radon seeds at a distance, and this had answered locally as satisfactorily as X-rays did.

? Darier-Roussy Sarcoid. Case for Diagnosis.—G. W. BAMBER, M.D. (for Dr. W. N. GOLDSMITH).

J. M., male, aged 25.

History.—In May, 1930, a painless swelling was noticed on the chest. More recently several new swellings appeared in its vicinity.

On examination, November 19, 1930, I found one nodule about 1 cm. in diameter, the skin over which looked slightly bluish. Grouped around this were some similar nodules over which there was no discoloration. They appeared to be situated in

the subcutaneous layer but to be firmly attached to the skin. From their situation and arrangement I thought that they might be Darier-Roussy sarcoids. There are now a large number of small nodules on the side and back of the trunk. I do not know whether these have appeared recently or were missed on earlier examinations.

Skiagrams of chest and of phalanges were normal. *Tuberculin reaction.*—Intradermic test was positive to 1 in 10,000 and negative to 1 in 1,000,000.

General medical examination revealed no abnormality apart from infected tonsils.

Blood-count.—R.B.C.s. 5,525,000; C.I. 0·85; W.B.C.s. 7,500. *Differential count:* Neutros. 55%; eosinos. 1%; large lymphos. 25%; small lymphos. 15%; hyal. monos. 4%.

The patient has been taking cod-liver oil and having general carbon-arc light baths but there has been little if any alteration in the nodules.

Biopsy.—The largest nodule, and the first to appear, was excised in November, 1930.

Histology.—The histological section seen with the naked eye shows presence of a very well-defined compact nodule situated chiefly in the subcutaneous layer but encroaching on the deeper layer of the cutis. Its upper boundary is very sharp and almost a straight line. The lower boundary is broken by several downward projections. Under the microscope the epidermis and greater part of the dermis are normal. The nodule is seen to consist of an infiltration of lymphocytes. These are disposed to a large extent in round islands, which correspond with connective tissue divisions of the adipose tissue. The lymphocytes are especially dense around the periphery of these islands, the centre being largely composed of young fibroblasts. There is a considerable new formation of fibrous tissue so that the fat cells are almost unrecognizable. The downward projections are seen to consist of sweat glands densely packed round with lymphocytes. These infiltrations are extraordinarily sharply circumscribed so that they almost give the impression of encapsulation. I am not sure whether the sweat glands are actually hypertrophied but they appear rather unusually large and conspicuous.

Comment.—Mr. W. G. Barnard says definitely that the swelling is not a neoplasm and doubts whether it is an inflammatory reaction, inclining to the view that it is more closely related to the deposits that occur in leukæmias. The blood-count does not reveal any leucocytosis; there is, however, a slight relative increase of lymphocytes, especially the large type. There is no enlargement of the spleen or lymph glands. The absence of epithelioid and giant cells distinguishes it from the typical structure of Darier-Roussy sarcoids. Possibly it is an example of the rather rare lymphomas which seem to occur quite independently of any blood disease. But those I have seen have been even more compact histologically and more like the Boeck's sarcoid clinically.

Discussion.—Dr. PARKES WEBER said he thought this belonged to the class lymphatic leukæmia, or, as the symptoms and signs at present were practically confined to the nodules in the skin, one would, on modern nomenclature, call it "*aleukæmic lymphadenosis, confined as yet to the formation of nodules in the skin.*" Even had the blood-count been normal he would have said the same. [Dr. Weber, however, on looking at the biopsy section a few days later desired to add that lymphosarcomatosis, an allied disease, could not yet be excluded.]

Dr. SEMON asked whether Dr. Weber anticipated that it would become a leukæmic blood-picture.

Dr. PARKES WEBER replied that it would not necessarily do so; the patient might die before that occurred, and not all such aleukæmic cases developed a typical blood-picture of lymphatic leukæmia.

Dr. SYDNEY THOMSON said Dr. Bamber had told him that this patient's tonsils were filthy. He had only seen four or five cases of aleukæmic lymphatic disease, but often they had begun with tonsillitis, and then two or three tumours of this kind formed. There was nothing special about the blood except a slight relative lymphocytosis. More and more tumours appeared quickly and the prognosis was hopeless.

Erythematous Lichen Planus, with Development of Bullæ.—LOUIS FORMAN, M.D.

Mrs. C. T., aged 35 (Dr. Barber's case).

No previous illnesses. Three months' history of eruption. Two days before the rash appeared she had sickness and diarrhœa, due, it may be, either to gastro-intestinal infection or to the development of lichen planus in the mucous membrane of the intestine. The whole of the skin of the back, from the neck down to the buttock, is erythematous and "tumified." The erythema is more patchy on the front of the chest, but is confluent on the abdomen down to the thighs. Small lichen planus papules are seen on the margins of the erythematous areas, and more typically on the front of the right wrist. Bullæ, of various sizes up to that of a shilling, have appeared on the thighs, developing on the erythematous areas.

I suppose this is not the type of lichen planus that one would treat with arsenic, either by mouth or intravenously,[1] and I would be grateful for the opinion of Members as to other methods of treatment, including lumbar puncture.

Discussion.—Dr. H. C. SEMON advised a trial of deep X-ray application to the mid-dorsal region before a resort to cerebrospinal puncture.

In a recent case, in which Dr. Gouldesbrough had used a 3- or 4-mm. filter, the result after one application had been extremely gratifying and had undoubtedly accelerated involution.

Dr. A. C. ROXBURGH said he had several times tried superficial X-ray therapy, but he had not found any benefit from it. It was said not to matter whether filtered or unfiltered rays were used. He had seen a fresh crop of lichen planus papules appear on the irradiated area. He had carried out lumbar puncture in several cases, but had never had any dramatic results from it. He had kept such patients in bed, and that perhaps explained such slight improvement as they showed.

Dr. W. J. O'DONOVAN said he had tried the application of both deep and superficial X-rays to the spine, and had performed lumbar puncture in over twenty acute severe cases, but without benefit from either treatment.

Dr. H. MACCORMAC said he understood that lumbar puncture was a form of treatment only suitable in acute cases with pronounced itching. In his first case the result had been most striking: in another, although no fluid was obtained, an equally good result was observed. In consequence he had no definite convictions as to the actual merits of this method of treatment.

Kaposi's Idiopathic Multiple Sarcoma, of Twenty Years' Duration.—LOUIS FORMAN, M.D.

M. Z., male, aged 58. Gives a history of the appearance of swellings on the dorsal regions of the feet, spreading up to the knees, which began twenty years ago. The hands and the forearms were affected at a much later date.

There is hyperkeratosis of the palms and soles. The skin of the feet and legs is purplish in colour, thickened, and crenated, and that of the legs is adherent to the tibia, owing to atrophy of the subcutaneous layer. On the back of the feet there are numerous soft tumours of varying size up to that of a pigeon's egg. These were shown on microscopical examination to be composed of dilated lymphatic vessels.

The patient complains of limitation of movement of the left knee due to the contracture of the involved skin behind it. The skin of the dorsum of the hands is purplish in colour and infiltrated. A similar area of infiltration is seen on the front of the left forearm. The general health is unimpaired and there is no evidence of visceral deposits. X-ray treatment was given ten years ago.

[1] I have since learnt that arsenic had been given to this patient by mouth by her private doctor before she came up to hospital.—L. F.

Microscopical examination of a section of the indurated area on the forearms showed some acanthosis and hyperkeratosis. The corium was fibrotic, and contained dilated thin-walled capillaries with collections of fibroblasts around.

The disease is showing a great tendency to spontaneous cure.

Peeling of Skin of Palms and Soles: Case for Diagnosis.—H. CORSI, F.R.C.S. (for Dr. A. C. ROXBURGH).

Patient, male, aged 39, has had peeling of the skin of the palms and soles fourteen times in five years. The attacks are preceded by erythema and pain. The process takes about three weeks and at the time the patient feels ill. The nails have also been cast in some of the attacks.

At present there are no physical signs other than a deep transverse furrow in the nails corresponding to an attack in November, 1930.

General examination: Wassermann and Mantoux reactions negative. Blood-count, normal.

Morphœa with Unusual Degree of Atrophy.—H. CORSI, F.R.C.S. (for Dr. A. C. ROXBURGH).

Patient, female, aged 22.

The condition began fifteen years ago and has become more and more extensive. It affects the trunk and is somewhat symmetrically distributed.

There are large sharply defined areas, brownish in colour, in which the skin is slightly depressed and translucent, so that the veins are clearly visible.

During the last two or three months two small patches of white-spot disease have appeared at the root of the neck, and on the abdomen there is a patch of morphœa with lilac-border, typical in appearance. The patient does not think that the brown patches of atrophy were preceded by scleroderma of any kind.

Discussion.—Dr. A. C. ROXBURGH said that when he first saw the patient there was no morphœa of the ordinary type. In all the cases of morphœa which he had seen, in which the patients had recovered, the skin had been restored to normal, and he was not familiar with this extreme atrophy following morphœa.

Dr. PARKES WEBER said that the second case illustrated one of his suggestions,[1] namely, that in considering any case of morphœic sclerodermia three types should be borne in mind: (1) where only the skin was affected; (2) where both skin and subcutaneous tissue were affected; (3) where only the subcutaneous tissue, with its fat, was involved, the last type being the rarest. Dr. Corsi's case began with patchy atrophic changes in the subcutaneous tissue, but now there were typical skin patches also. The term sclerodermia was in reality a misnomer for the third type, because the change was of an atrophic nature in the subcutis (and ? deeper cutis). In fact, it was neither sclerotic nor chiefly dermic. The three types might be associated in various ways with each other, and might also be associated with a remarkable telangiectatic condition of skin or with cutaneous pigmentation. Every variety of morphœic sclerodermia might be fitted into this scheme.

Parapsoriasis en plaques.—Sir ERNEST GRAHAM-LITTLE, M.D.

Patient, male, aged 31. Lupus erythematosus of the face developed during the late war. There is some scarring from the result of treatment of the patch by freezing with carbon-dioxide snow. On some date succeeding this development, but before the end of the war, he began to suffer from large patches of a dry scaly eruption which has persisted ever since that date. The eruption is symmetrical, covering large areas of the trunk and limbs, and is a typical instance of parapsoriasis.

[1] Cf. F. P. Weber's remarks, *Brit. Journ. Derm. and Syph.*, 1930, xlii, pp. 336-337.

Sclerodermia.—Sir ERNEST GRAHAM-LITTLE, M.D.

Patient, female, aged 24, suffering from a very extensive sclerodermia affecting the greater part of the surface of the body and limbs. There is extreme emaciation owing to contraction of the affected skin over the bones, and the left leg has become permanently flexed at the knee-joint, almost at a right angle to the thigh. She showed extensive septic intoxications of the antrum and the bowel, with *Streptococcus viridans*. The disease has lasted for six years and is causing a progressive deformity.

Postscript.—The knee-joint was found to be completely disorganized and since showing the case the leg has been amputated with a very successful result.

Neurotic Excoriations.—Sir ERNEST GRAHAM-LITTLE, M.D.

The patient is a woman, aged 45, with extremely numerous superficial excoriations scattered almost over the whole surface of the body which can be reached by the hands, and it is remarkable how far she has in fact been able to mutilate herself by scratching. She would seem to be ambidextrous, and at any rate can produce lesions of nearly equal severity by both hands. She has a general pruritus, the cause of which is rather obscure and which has persisted for twelve years. She had an early menopause three years ago, and has always been a highly nervous person. She is, at the present time, under the care of my colleague, Dr. Gosse, on account of neurasthenia. She had a floating kidney removed some years ago; the operation scar is seen on the right side.

Postscript.—Since the meeting the patient has been taken into St. Mary's Hospital and it has been established that she produces the lesions herself by digging out from the skin with her nails what she calls a "worm-like" body, but which is really a portion of the epidermis. There are numerous scars resulting from previous excoriations, as well as extensively-distributed fresh lesions in an active condition. Under treatment, which has consisted simply in securing the hands so that she cannot scratch herself, and in giving nerve sedatives, the condition has greatly improved. There are no fresh lesions since she has been in the hospital and the excoriations have healed completely, but she still complains of intense general itching.

Clinical Section.

[*February* 13, 1931.]

Sarcoma of the Orbital Roof Treated with Radium.—CECIL P. G. WAKELEY, F.R.C.S. (President).

About five years ago Sidney J., aged 17, noticed that right eye was rather larger than left. Since then right eye has gradually become more prominent. Vision of affected eye always somewhat better than that of the other. Never any pain in right eye, or headache or diplopia.

First attended King's College Hospital February, 1930. Since then condition has advanced slightly.

On examination.—Right eye markedly proptosed and displaced downwards and slightly outwards (fig. 1). Upper border of right globe on same level as lower border of left globe. Slight epiphora. Movements of the eye good in all directions, except upwards, where it is slightly impaired. Lachrymal gland seen clearly on everting upper lid. Pupil similar in size to opposite one; reacts to light and accommodation. Consensual reflex present. Both eyes myopic, right less so than left. Without glasses vision in right eye is $\frac{6}{12}$, in left eye $\frac{6}{6}$. With a

FIG. 1.—Displacement of right eye due to sarcoma of orbital roof.

$-1{\cdot}00$D and $-1{\cdot}75$D lens respectively, vision in each eye is $\frac{6}{6}$. Media clear; both fundi appear normal; visual fields normal. In upper part of the orbital cavity a smooth hard mass can be felt, apparently projecting from roof of orbit.

Other systems normal; liver not enlarged; no evidence of secondary deposits in lungs.

An X-ray examination, 1930, showed marked exposition of wall of right frontal sinus and depression of upper orbital margin. On the X-ray findings a tentative diagnosis of mucocele of the frontal sinus was made; on February 25, 1930, my colleague, Mr. V. E. Negus, explored the sinus. On his opening the sinus, a quantity of colourless fluid under pressure escaped. The sinus was lined by what appeared to be a degenerate epithelium. The cavity was much larger than normal (one inch and a half to two inches in depth). The posterior wall of the sinus was deficient,

and the meninges could be seen. There appeared to be some smaller cysts on the lateral wall.

Report of microscopical examination on portion of cyst wall.—" The wall of the cyst consists of neoplastic tissue, probably sarcomatous, infiltrating the surrounding bone. It is very cellular, and the cells are of the fibroblastic type, spindle-shaped and with large nuclei which do not show a very definite nuclear membrane, a very fine chromatin reticulum and no

FIG. 2.—Lateral skiagram of skull showing radium needles in the sarcoma.

nucleolus. . . . . The stroma is not very marked. . . . . There are small islands of bone undergoing absorption. . . . . The growth, judging from the absence of mitotic figures, is not very active."

The condition has been treated with radium. On March 10 and April 4, 1930, a tube containing 8 mgm. of radium was applied for 68 hours at a time. On January 30, 1931, 11 mgm. in milligram tubes was inserted for 99 hours (fig. 2).

Wassermann reaction, negative. Blood-count (March, 1930), normal: R.B.C.s, 5,200,000; Hb., 100%; W.B.Cs., 9,600. *Differential.*—Polys., 72%; lymphos., 22%; large hyalines, 2%; eosinos., 1%; basophils., 1%.

The orbital margin has completely gone, and therefore the eye is now tethered solely in the periosteum lining the orbit. Although the tumour is very vascular, it seems to be growing slowly.

Four Cases of Paget's Disease of Bone Complicated by Fractures.—A. D. MORRIS, M.B. (introduced by the PRESIDENT).

I.—C. M., male, aged 55. On July 24, 1930, patient stumbled over a bucket. Admitted to hospital same day. Skiagram showed transverse fracture of left femur about an inch and a half below lesser trochanter. Treated by extension in

CASE I.—C. M. Paget's disease. Skiagram of left femur, showing union after refracture.

a Thomas's bed-splint. Twelve weeks later, fracture having united satisfactorily, patient was beginning to get about in a walking calliper. On October 20 he turned over in bed suddenly and refractured the femur at the site of the original fracture. A Steinmann's pin was inserted through the lower end of the femur and a weight extension applied. Union is now quite firm, and he is getting about satisfactorily in a walking calliper.

Skiagrams show changes characteristic of osteitis deformans in several bones, including the fractured bone.

II.—L. B., female, aged 66. Bowing of legs first noticed fourteen years ago. Boring pain in legs for past eight years. On October 17, 1930, when she was walking with the aid of a stick, the stick slipped and she fell to the ground, her right leg being doubled up under her. Admitted to hospital ten days later. Skiagram showed transverse fracture of right femur at junction of middle and lower thirds, together with marked changes of osteitis deformans throughout the whole femur. The fracture united rapidly in good position. On December 12, 1930, patient was being helped out of bed for the first time since her accident, and had just put her sound leg on to the ground when a snap was heard, and her leg gave way, but she was caught before reaching the ground. Skiagram of leg showed incomplete transverse fracture of tibia, without separation or displacement of the fragments, resembling a greenstick fracture. Osteitis deformans changes were also present in this bone. For a short time after the injury a hæmatoma-like swelling was present over the site of the fracture.

Union is now firm and satisfactory. She has not yet walked since her accident. Skiagrams show changes of osteitis deformans in many other bones, and calcification is present in the ischial bursæ. Patient has an interesting swelling (? calcified mass) on the left side of the abdomen, just above the iliac crest.

III.—H. H., aged 64, a night watchman, was knocked down by a motor-car May 6, 1930. Front wheel of car struck his right thigh, and back wheel passed over his right leg. Skiagram of the leg showed a transverse fracture of the middle third of the right femur, and a compound fracture of both bones of the leg in the lower third. Treatment by Thomas's bed-splint, with extension. Patient became mentally deranged for a time, and kept removing the splint and tearing off the dressings. Fracture of femur united early and satisfactorily; fracture of tibia and fibula united late and with considerable deformity. Patient was discharged from hospital, using crutches, and was to return later for correction of deformity of leg, but a few days afterwards at home he upset a pail of boiling water over his injured leg, and was readmitted to hospital December 23, 1930. Pneumonia developed later, and patient died on January 5, 1931. Skiagrams showed changes of osteitis deformans in the lower part of the affected femur only, all other bones were normal. The specimen shown consists of the right femur which has been cut in longitudinal section after immersion in Kaiserling's solution. The fragments had united with a great deal of new bone formation around the site of fracture. The lower fragment is broadened, the cortex is enlarged, and the medullary cavity filled with numerous cyst-like spaces. I believe that this is a case either of osteitis fibrosa or of a parathyroid tumour.

IV.—H. A., male, aged 53, a carman, on October 29, 1930, tripped while walking and his leg gave way under him. Admitted to hospital same day. Skiagram showed transverse fracture at junction of upper and middle thirds of femur, and changes of osteitis deformans affecting the whole bone. A Steinmann's pin was inserted through the tubercle of the tibia and weight extension applied. Fracture united rapidly and satisfactorily, and the splint was finally removed December 12,

1930. About this time the patient developed acute mania and had to be transferred to a mental hospital, where he is still an inmate. In this case the femur was not the only bone affected with osteitis deformans.

In all these cases the direction of the break was transverse. I was surprised at the rapidity with which union occurred in all the cases, even after the re-fractures; in three of the cases the fractures were spontaneous. In one case there was a calcified mass above the left iliac crest and calcification was present in the ischial bursæ. The Wassermann reaction was negative in all cases, and the blood-calcium estimated in two cases was normal. An excessive amount of callus had formed in three cases. The functional result was good in all.

The PRESIDENT said he thought it questionable that the case from which the specimen shown had been obtained was one of Paget's disease. At the autopsy the thyroid had been examined thoroughly; the parathyroids were normal, thus excluding the probability of osteitis fibrosa.

He could not explain the calcareous mass under the left iliac spine; there was no bursa. He could only think it was a hæmatoma which had become calcified.

Gangrene of the Foot in Diabetes.—BERNARD MYERS, C.M.G., M.D.

Mrs. F., aged 55. Complained of ulceration of the left foot and was admitted to Royal Waterloo Hospital, May, 1930.

Six months' history of thirst, increased appetite, and polyuria. Some dimness of vision of right eye.

Condition on examination.—Diabetic facies. Perforating ulcer on left hallux, where bone was exposed for about an inch.

Urine: Sugar, + +; acetone, + +; sp. gr., 1020; 31 oz. per day. A few R.B.C.'s and W.B.C.'s seen. Blood-sugar, 0·17 to 0·18%. Wassermann reaction, negative.

Retinitis in right eye; some small hæmorrhages and exudative areas. In left eye, opacities (lenticular).

Treatment.—Dietetic; 5 to 10 units of insulin twice daily. Incision of toe.

In just over two months the toe had completely healed up and patient left hospital sugar-free, feeling well, and able to walk without difficulty.

Purpura Gangrenosa in Diabetes.—BERNARD MYERS, C.M.G., M.D.

Mrs. L., aged 48. Attended hospital December, 1930, on account of ulcerated leg. A rash had been present on the leg for a month previously, first appearing as rounded purple areas from a quarter to one inch across, some tending to increase in size; ulcers formed in the centre of these spots.

Dr. Thompson Barron diagnosed rash as purpura gangrenosa of the legs.

Urine (24 hours' specimen) contained 0·7% of sugar. Blood-sugar, 0·27%. Blood-count: R.B.C.'s 4,750,000; Hb., 92%; C.I., 0·096; W.B.C.'s, 6,200. *Differential count* normal. Platelets, 232,000. Wassermann reaction, negative.

Treatment.—Dietetic; insulin, 15 units, twice daily. Radiostoleum applied locally to ulcers.

General condition has greatly improved; urine is sugar-free, and ulcers are healing satisfactorily.

Arterio-sclerosis is present—but not markedly—in both this and the previous case. The patient has been instructed as to the necessity of keeping the foot clean and wearing an extra sock to prevent injury. The diet contained carbohydrate 40 grm.; protein 60, and fat 120, the whole equivalent to 1,480 calories. The patient is still having insulin, 5 units twice daily, and keeps well. The relation of insulin (units) to carbohydrate (grams) is 1 to 4.

Discussion.—The PRESIDENT asked whether radiostoleum was a specific for these ulcers.

Dr. MYERS (in reply) said that radiostoleum was used because it contained vitamin D. The ulcers to which it was applied had healed well.

Diabetic Coma in a Boy.—BERNARD MYERS, C.M.G., M.D.

Edmund A., aged 6. Admitted to hospital last July with coma. There was a history of anorexia, wasting and cough for three months.

Condition on examination.—Child comatose, with marked air-hunger; body wasted and pigmented; temperature, 97° F.; pulse, 110; respirations, 26. Slight impairment in each supraspinous fossa.

Urine contained slight amount of albumin; sp., gr. 1040; sugar, 1% +; acetone markedly present.

Blood-sugar, 0·085%, ten days after admission and treatment commenced. Wassermann reaction negative.

Family history.—Three other children in family; all well. Mother has tuberculosis.

Previous history.—Tonsils and adenoids removed a month before admission.

Treatment.—Ten units of insulin were given twice daily at first, but this was reduced to four units twice a day and then once a day. The coma quickly yielded to the insulin, dietetic treatment, and alkalies.

Patient kept well on a diabetic diet and an injection of insulin once daily, although he has been free from all symptoms on various occasions for three or four days at a time without insulin. At present he has 5 units of insulin twice daily.

Upon admission to hospital, he was given 10 grm. of glucose in orange juice by the mouth, and 10 units of insulin subcutaneously. This was repeated in an hour and a half, after which consciousness returned completely and symptoms disappeared.

The diet contained 41 grm. of carbohydrate, 114 grm. of protein and 93 grm. of fat, equivalent in all to 1,460 calories daily. One unit of insulin is being given at present for every 4 grm. of carbohydrate. The protein is to be reduced and the carbohydrate cautiously increased.

This boy has gained 14 lb. in weight in seven months, i.e., since the diabetic coma last July. Jocelyn states that these children gain in weight quite well and that sexual development is normal, but that growth in length is less than normal. That is so in this case.

Dr. MYERS, in answer to a query by Dr. Stolkind as to what became of these cases in the past before insulin treatment, said that so far as he knew the patients all died, and some very quickly.

Spontaneous Lactation with Enlargement of the Pituitary Fossa.—DAVID KRESTIN, M.D.

D.K., aged 25, female, single. Has never been pregnant.

Past history.—Uneventful; has always been healthy.

Family history.—Both parents, brothers and sisters all healthy, tall and well built.

Present history.—For past two years catamenia have become irregular and scanty, after always having been regular since age of 14.

Seventeen months ago catamenia ceased completely. Some months later patient noticed that breasts seemed larger and heavier than previously. Six months ago her attention was directed to secretion from nipples by staining of clothes. Pressure of either nipple has always produced a copious milky fluid, which has never been blood-stained. No pain, apart from a feeling of fullness or heaviness in the breasts.

For some years past there have been headaches, usually frontal, occasionally temporal; as a rule coming on in mornings; more severe during last twelve months, but of very short duration. Vision and hearing good. No vomiting.

Has always been tall and well built, but thinks she has lately been getting bigger and heavier. No change in size of hats, gloves or shoes. Has noticed that skin is becoming coarser and that arms and legs are more hairy.

On examination.—Well built and healthy looking. Weight (13.11.30) 12 st. 8 lb. Height 5 ft. 11 in.

No undue prominence or enlargement of the bony ridges of skull, lower jaws, hands or feet. Conformation of hard palate, teeth and alveolar margins normal. Radiograms of hands show no abnormality of phalanges. Skin of arms and legs somewhat coarse and fairly hairy.

Pupils equal: react well to light and accommodation. Fundi normal. No ocular palsies. Visual fields for white are normal, those for red and green are rather contracted, but within the limits of normal (Mr. A. Sorsby).

Other cranial nerves normal. No abnormality detected in nervous system. Cardiovascular system healthy. Blood-pressure 120/80.

Chest clear. Abdomen, liver and spleen not felt; no tumours can be palpated. Linea atrophica not present. Pelvic organs normal; hymen intact.

Both breasts are enlarged, heavy and somewhat nodular, resembling those of a lactating woman; the skin over them shows a few enlarged superficial veins. No tumour can be felt. Compression readily yields a secretion resembling milk. A test-tube can be filled by the patient in two or three minutes, from either breast.

Qualitative analysis of the fluid shows presence of fat, lactose and casein, as found in human milk. Microscopically, the centrifugalized deposit contains numerous fat globules, a few leucocytic cells and many granules resembling colostrum corpuscles. No leucocytic excess.

Urine: 40 oz. in twenty-four hours. Sp. gr., 1022. No albumin or sugar.

Sugar metabolism: Blood-sugar curves after ingestion of 50 grm. and 100 grm. of glucose respectively, were within normal limits. No sugar appeared in urine during these tests. Wassermann reaction, negative. Blood-count normal. Cushing's thermic reaction, negative. Skiagram of skull (Dr. M. Schwartzman) showed no obvious deformity of lower jaw and no enlargement of air sinuses. The sella turcica is enlarged in depth and in antero-posterior diameter. Measurements of fossa: antero-posterior diameter 21 mm., greatest depth 17 mm., which exceed Cushing's maximum measurements for a normal fossa, viz., 15 mm. and 10 mm. respectively.

Discussion.—The PRESIDENT said that probably this was a case of acromegaly, and that in a short time the lower jaw would become definitely enlarged; the approximation of the teeth would show this. He did not think the application of deep X-rays was of any use in cases of pituitary growth unless a decompression operation had been first performed and the X-rays directed through the hole in the skull. If there was actually a pituitary tumour, the best method of treatment would be the introduction of radon seeds into it.

Dr. F. PARKES WEBER thought the enlargement of the breasts in this case might be analogous to the enlargement of various viscera, which was a well-known, though rather rare, symptom of acromegaly. This, he thought, was the correct diagnosis.

Encapsulated Intrathoracic Tumour.—DAVID KRESTIN, M.D.

P. McM., male, aged 6. An only child. Admitted to Prince of Wales' Hospital 29.12.30, under care of Dr. Bruce Williamson.

Family history.—Nothing of note.

Past history.—Full term child, normal labour. Twenty-four hours after birth had an attack of "suffocation" when he turned blue, and oxygen had to be given.

Similar attack at age of three months, after which he was admitted to a hospital. Skiagram of chest revealed enlargement of thymus with collapse of right lung (mother's history). Continued to have attacks of dyspnœa, and at age of 4 years had an acute pyrexial illness first diagnosed as a pneumonia of the left lung and then as a left-sided pleural effusion. Chest condition improved but no record of a subsequent examination. Has always been difficult, weakly and under-nourished. Whooping-cough at age of 3 years ; no other infectious diseases.

Three months before admission an acute pyrexial illness developed, accompanied

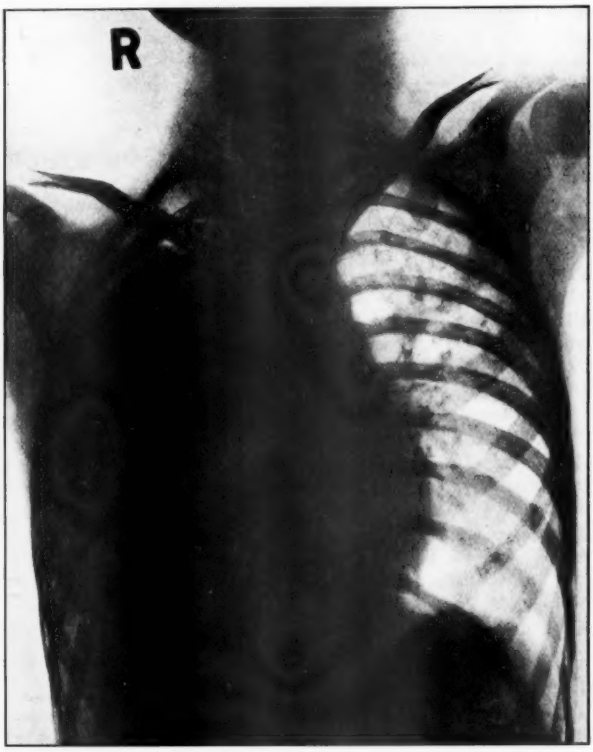


FIG. 1.—Antero-postero radiogram of chest after injection of lipiodol, showing filling of bronchi to right upper lobe, absence of oil in bronchi of right lower lobe, and lateral distortion of lower end of trachea.

by cough and laboured breathing. Pneumonia of right lung was first diagnosed, but later a pleural effusion of the right chest was suspected. The temperature became normal after three or four days, but the physical signs in the chest remained abnormal up to the time of admission.

On examination.—Thin, pale, under-nourished boy. Palpebral fissures of equal size; pupils dilated ; equal ; brisk reaction to light and accommodation. Other cranial nerves normal. Tonsils large and red. A number of superficial, small, soft and discrete lymph nodes up to the size of a small pea in both posterior triangles of neck and both axillæ. Trachea not displaced.

Chest somewhat " pigeon breasted " in type, with a prominent sternum. Right side flattened in infraclavicular region. No bulging or obliteration of intercostal spaces. Movements restricted over whole of right side, but especially so in axillary and basal zones.

Cardiac apex is felt during expiration in the fourth left interspace $\frac{3}{4}$-in. internal to mid-clavicular line. During full inspiration pulsation is felt in third and fourth interspaces to right of sternum. Left border of heart $\frac{1}{4}$-in. internal to line of apex beat during expiration, but during inspiration is in mid-sternal line. Cardiac sounds clear · second pulmonary somewhat accentuated. Percussion note over left chest slightly hyper-resonant. Over right chest it is high pitched and flat

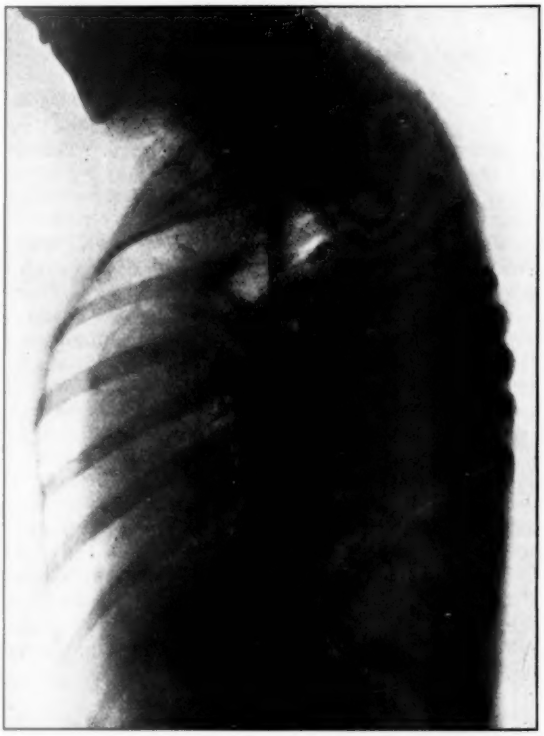


FIG. 2.—Lateral radiogram showing margins of tumour arising from the posterior mediastinum.

in infraclavicular region, becoming hyper-resonant as well as high pitched in inframammary region, and completely dull in axilla. Dull zone in axilla well defined, extending forwards to anterior axillary line, posteriorly to vertebral border of scapula and downwards to sixth rib. Posteriorly below this level, percussion note is definitely impaired but not absolutely dull.

On auscultation, breath sounds over left chest loud and vesicular. Over right chest they are loud and bronchial with prolonged expiration, over infraclavicular region, absent over dull zone in axilla; greatly diminished over right lower and middle lobes. A few fine consonating crepitations heard over right base.

Tactile vocal fremitus and vocal resonance increased over right infraclavicular region, but diminished in axilla and over base.

Abdomen presents nothing abnormal. Liver dullness extends to seventh rib anteriorly and eighth rib in mid-axillary line; it is not palpable.

No clubbing of the fingers or toes.

Report on radiological examination (Dr. DIXON).—On screening, right chest is opaque up to level of third rib anteriorly. Cardiac shadow drawn over to right with each inspiration. Figs. 1 and 2 show dense homogeneous shadow filling right mid-zone with well defined convex upper margin at level of third rib. Below level of sixth rib, opacity becomes less dense. In lateral view, denser shadow has ill-defined lower margin at level of the sixth rib where it is separated from the lighter shadow below. Cardiac shadow drawn over to right. Intra-tracheal lipiodol shows filling of bronchus to right upper lobe, but not of that to right lower lobe.

Right chest was explored with needle and syringe; no fluid could be obtained in any of spaces.

Blood-count (9.1.31).—R.B.C.'s, 4,560,000 per c.mm.; W.B.C.'s, 6,875 per c.mm. *Differential.*—Polys., 62%; large lymphos., 14%; small lymphos., 20%; hyal., 2%; eosinos., 2%. Intracutaneous tuberculin reaction negative. Temperature normal, except for occasional rises. One such rise lasting from January 16 to 23, 1931, was associated with discharge from right ear, enlargement of lymph nodes on right side of neck, and a leucocytosis. There was a slight cough, but no alteration in physical signs. There is usually no cough and no expectoration.

Urine clear. Wassermann reaction negative. Investigation up to the present would indicate presence of a solid, circumscribed tumour in mid-zone of right chest, compressing bronchus to lower lobe, which, as a result, is partially collapsed. Clinical and radiological examinations suggest that this tumour arises either from posterior mediastinum or from peripheral pleura. The history suggests a condition of long standing, or possibly present at birth.

The tumour has been present for a long time although not recognized previously. At first I thought that probably it would be a dermoid. But in only nine out of 135 cases of dermoids and teratomata, collected by Heuer, the patients were under 12 years of age. Moreover, most dermoids arise in the anterior mediastinum, whereas apparently this arises in the posterior mediastinum. Fibroma is very rare in children. In another paper, Heuer draws attention to a case like this, except that there is no collapse of the right base. It was successfully removed, and on examination it was described as an endothelioma of the pleura. Ganglion neuromata have been removed from children without having given definite manifestations for some time, until a picture like this was produced. They occur in young individuals early in life, and arise in the upper part of the posterior mediastinum. Nine cases have been collected, with two successful operations.

Discussion.—Mr. W. IBBOTSON said that the injection of lipiodol through a bronchoscopic tube was a better method of getting lipiodol into the bronchus than that of putting a needle into the trachea. In the case under discussion, one could see the constriction of the bronchus and could then put in the lipiodol at the same time whilst the patient was on the X-ray table.

Dr. BURTON WOOD said that at present he had under his care a similar case in a boy, aged 13. He had had a tumour very like the one now shown, with a clearly-defined upper margin extending almost to the level of the third rib. Artificial pneumothorax was performed and cleared up the margin of the tumour which was found, on needling, to be firm and hard. The boy was in perfect health. There had been no change in the size of the tumour during the last year, and as it had evidently been there since early childhood, he (the speaker) was loth to advise an operation.

Dr. ANTHONY FEILING said that he had recently had a case which proved to be one of ganglioneuroma and he suggested that this might be the same. The skiagram was similar.

In his case the patient, a boy aged 4, had been admitted to hospital on account of paraplegia, thought to be due to spinal compression. A skiagram was taken, in the belief that there was something wrong in his vertebral column. There was an almost globular shadow in the thorax, mostly on one side, but spreading across the mid-line in the mid-thoracic region. The boy had no pulmonary symptoms at all. Eventually he was operated upon, and the tumour was found to be extra-pleural, and removed.

Dr. KRESTIN (in reply) said that an artificial pneumothorax had been intended, but the boy's family were unwilling for him to undergo an operation. The growth of the tumour had not altogether ceased. In the case of Sauerbruch's, of which he showed a slide, the growth was a ganglioneuroma, and had been successfully removed. He agreed this tumour might be of that nature.

Five Cases of Thrombo-Angiitis Obliterans treated with Muscle Extract.—M. SCHWARTZMAN, M.B.

(I) *Combined Thrombo-Angiitis Obliterans and Reynaud's Disease.*

J. J., miner, aged 43. No history of venereal disease.

History.—Early in 1922, intermittent claudication.

End of 1929.—Attacks of white dead appearance of all toes and of fingers, followed by intensely blue colour and associated with severe burning sensation.

Affected parts became cold, blue and swollen. Within a few months tips of eight fingers and all toes except one fell off.

December, 1929.—Burning sensation became unbearable and black offensive discharging ulcers appeared on stumps of the self-amputated parts.

11.6.30.—Admitted to Guest Hospital at Dudley (Dr. C. Walker). Unbearable burning pain. Deep gangrenous patches on stumps. Sleeplessness. Cachectic appearance. Posterior tibial and dorsalis pedis arteries were imperceptible on both sides.

Right radial artery felt ; left, pulseless.

Postural colour changes, slight.

X-ray examination showed necrotic changes at terminal phalanges of fingers and toes. No calcification of arteries seen. Blood-pressure, 130/100.

Treatment with muscle extract begun 15.6.30, and continued till 8.8.30.

Treatment restarted in November, 1930, and still continued with intervals. Pain disappeared. Discharge stopped. Gangrenous patches displaced by healthy granulations. Blood-pressure fell to 100/60.

(II) D., a clerk, married, aged 43. No history of venereal disease. Moderate smoker. Wassermann reaction of blood and cerebrospinal fluid negative.

1919, intermittent claudication.

1926, shooting pains in left foot.

January, 1927, ulcers broke out on right foot.

April, 1927, periarterial sympathectomy right femoral artery (Mr. G. Mullally, Westminster Hospital). Gangrene of right little toe a fortnight after operation.

April, 1927, amputation of right foot above ankle (Mr. G. Mullally).

May, 1930, readmitted to Westminster Hospital with advanced gangrene of the left toes. Soft tissues of big toe partly sloughed off. Also black ulcers on two or three toes. Foot swollen, stone cold, deeply blue. Offensive discharge. Distal portion of left big toe necrosed. Amputation stump (right) ulcerated. Left dorsalis pedis and posterior tibial arteries pulseless. Severe continuous pain. Blood-pressure, 155/130.

Daily injections of skeletal muscle extract till beginning of July, 1930. Pain ceased, swelling subsided. Discharge disappeared, colour improved, surface of the

foot became normal. Healthy granulations appeared. Blood-pressure, 130/90. Treatment continued for another three months. Wounds completely healed. No pain or discomfort. Patient can ride a bicycle for a few hours a day.

(III) Patient, male, aged 41. No history of venereal disease or alcoholism; smokes 20 cigarettes a day.

Since April, 1929, severe crampy pain in the thighs on walking. The distance he could walk without pain gradually decreased from half a mile in April to 40 yards in September, 1929.

Restriction of smoking, rest, reducing diet (lost 2 st.), and medicinal treatment failed to alleviate pain.

January, 1930, admitted to Westminster Hospital (under Sir James Purves-Stewart).

The posterior tibial arteries were faintly felt on both sides. Both dorsalis pedis arteries were pulseless. Movement of right leg against resistance or on elevation to 180° caused blanching.

X-ray examination of both legs revealed no calcification of arteries. Blood-pressure 165/90. Wassermann reaction, negative.

Treatment with muscle extract began in January, 1930. At the end of a monthly course patient could walk half a mile, at the end of which he felt weariness of legs but no pain. Blood-pressure, 130/90.

Patient has been under observation for one year, having occasional treatment (once or twice a week). Improvement maintained. Crampy pains never recurred. Ability to walk without weariness of legs varied from two miles during summer to quarter or half a mile in autumn and winter in bad weather. Blood-pressure, 115/70.

Pulses in posterior tibial arteries felt well; in dorsalis pedis, doubtful.

(IV) T. J., a mechanic, aged 42. No history of venereal disease. Moderate smoker. Since 1924, intermittent claudication. 1926, trophic disorders on right foot and toes. Early 1929, gangrene of right foot. Amputation below the knee (Mr. C. Price Thomas at Westminster Hospital).

A fortnight afterwards re-amputation above knee (Mr. Tudor Edwards). December, 1929, gangrenous changes on left big toe.

January, 1930, periarterial sympathectomy of both left femoral and tibial arteries (Mr. E. Rock Carling at Westminster Hospital).

July, 1930, readmitted to Westminster Hospital in condition of advanced gangrene of left foot and toes. Soft tissues of left big toe were black, sloughing—hanging in shreds. Offensive discharge. A black area extended alongside bases of toes. Foot much swollen and cold. Patient suffered excruciating pain. Left dorsalis pedis and posterior tibial arteries pulseless. Amputation stump of right thigh ulcerated. Wassermann reaction of blood, negative. Blood-pressure, 135/90.

Treatment with muscle extract begun 5.7.30 at Westminster Hospital (under Mr. Carling), and continued at London Jewish Hospital (under Mr. S. I. Levy) till middle of October. Pain and discharge gradually ceased. One and a half terminal phalanges of big toe separated. Œdema disappeared. Colour improved. Blood-pressure, 125/70. Wound healed up. Arteries pulseless as before treatment. No change in oscillometric index.

(V) B. L., tailor, aged 41. No history of venereal disease or alcoholism.

Since 1916 attacks of superficial phlebitis.

Since 1924 frigidity and cyanosis of right leg; sensation of numbness even when at rest. Intermittent claudication.

Condition of arteries as recorded at the London Hospital in 1926:—Left femoral:

Pulsation greater than in right. Right popliteal: posterior-tibial, anterior dorsal not felt.

Intermittent claudication became gradually worse and ability to walk without pain was reduced in April, 1930, to twenty yards. Posterior-tibial and anterior-dorsal not palpable on either side. A permanent intensely red patch (chronic erythromelalgia) appeared along bases of right toes. Dead white appearance of foot and toes chiefly on right side on elevation; induced rubor in dependent position.

Treatment with muscle extract for four months.

The patient is able to walk about two miles without pain or tiredness. Legs and feet warm. The right leg is now warmer than the left. Blanching on elevation, and induced rubor in dependent position are much less marked. Patch of chronic rubor has almost entirely disappeared.

Patient has now returned to his work, which he had had to give up over a year ago on account of his disease.

Discussion.—Dr. PARKES WEBER thought that Dr. Schwartzman's results with muscle extract (like some recorded from angioxyl) seemed hopeful. But the course in cases of thrombo-angiitis obliterans before the introduction of angioxyl, etc., had sometimes been most unexpectedly good. Thus a man, demonstrated by the speaker during the first year of the Royal Society of Medicine (Clinical Section, December 13, 1907), was still living, and possessed and could use his legs and arms, though he still had a certain amount of intermittent claudication. Both lower limbs and one upper limb had been affected. At one time the pain from superficial ischæmic ulceration (threatening gangrene) of the foot had been very severe, notably at night. The patient had been free for the last (many) years from any signs of active recurrence of the disease. (See F. P. Weber, *Lancet*, 1908, i, p. 152, and 1925, ii, p. 21). Dr. Weber had seen this patient recently. Though there was no family history of the same disease two of his children developed grave diabetes in youth and died, and a grand-daughter suffered during infancy from typical attacks of Raynaud's syndrome, about fifteen in the month, for many months.

Dr. SCHWARTZMAN, in reply, said that Dr. Parkes Weber's remarks, as well as his own experience, showed that one should not be in a hurry to agree to amputation. Nobody knew whether this was a progressive disease which never stopped, or whether there might be some cases in which the circulation was sufficiently compensated.

Another method of treatment, suggested in America by Brown and Allen, was the use of T.A.B. vaccine, which also seemed to be useful. It was said that there occurred a rise of systemic temperature which caused a local rise of temperature, and some adjustment of the vasomotor mechanism. It had shown some good results, but it was not sufficient, because the authors said that if there were one or more digits which mortified, the only treatment was amputation. Muscle extract could be used with advantage in such cases, and this treatment was certainly better than surgery.

Two Cases of Pulmonary Asbestosis.—PHILIP ELLMAN, M.R.C.P.

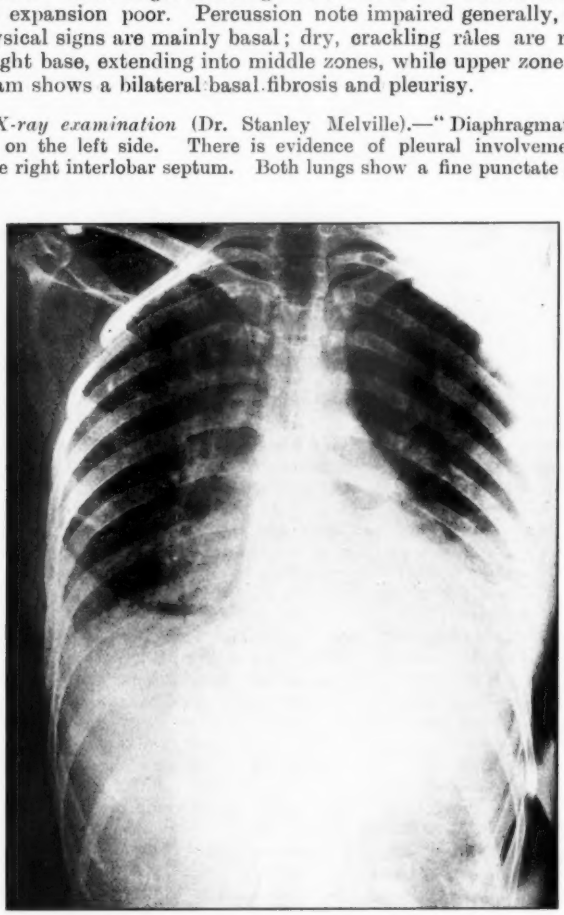
(I) C. N., female, aged 28, single. Asbestos worker from 1921 to 1926, engaged in making mats. The work involves the production of a considerable amount of dust. Never had any chest trouble until three years ago, i.e., after having been engaged in the industry for seven years. Then developed a cough, with some shortness of breath on exertion; cough and dyspnœa have become progressively worse. Patient complains of readily "catching colds," with corresponding aggravation of the symptoms. During these colds has had severe "stabbing pains," worse on inspiration, at both right and left bases. Cough usually "hard and dry," but, as a rule, there is a little mucoid sputum (1 drachm) during the day. Sputum has never been blood-stained. Frequently has night sweats, sometimes sufficiently severe to awaken her during night and make her dry herself. At present is free from cold; appetite is good; feels comparatively well.

No previous illnesses; no history of tuberculosis in family.

Has lost about 6 lb. in weight since first seen in August, 1930. At times some degree of cyanosis. Some finger clubbing and evidence of old asbestos "corns" on hands. Chest expansion poor. Percussion note impaired generally, but especially at bases. Physical signs are mainly basal; dry, crackling râles are readily heard, especially at right base, extending into middle zones, while upper zone is free.

The skiagram shows a bilateral basal fibrosis and pleurisy.

Report on X-ray examination (Dr. Stanley Melville).—"Diaphragmatic movements poor, especially on the left side. There is evidence of pleural involvement. There is thickening of the right interlobar septum. Both lungs show a fine punctate mottling at the bases with some fibrosis. (See fig.) The appearances are characteristic of a trade pneumokoniosis."



Note characteristic fine mottling at both bases with some fibrosis. Heart is drawn well over to the left, and the costo-diaphragmatic angle is obliterated. (Dr. Ellman's first case).

Sputum examination (Dr. N. H. Schuster).—"A fairly clear mucous specimen which is only slightly viscid and contains mucous strands. Pus cells are scanty. The majority of the cells are granular mononuclears, probably phagocytes. No bronchial epithelial cells seen."

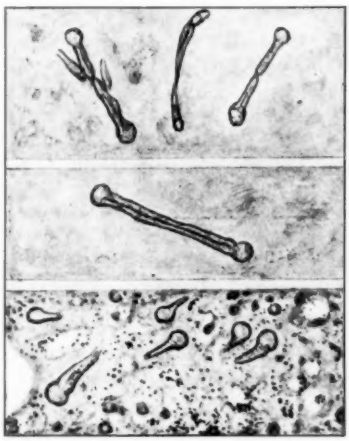
"Organisms are scanty and *B. tuberculosis* are not found. Asbestos bodies and fibres are present in large numbers."

(II) S. L., female, aged 34, married, has been engaged in an asbestos factory from 1911-17. Has had a slight cough "on and off" for years. The cough began to trouble her seriously only about nine months ago, when she re-commenced work at

the factory, i.e., about 18 years after first being employed there. With the cough she has had dyspnœa which has become progressively worse and is now quite marked on exertion. During last few months has had "frequent colds on the chest" with marked aggravation of all symptoms. Has not lost much weight since first seen in September, 1930.

She has a "hacking" cough with some muco-purulent expectoration (½ oz. in 24 hours); sputum has never been blood-stained; has severe night sweats; appetite poor; complains of lassitude; evidence of old "asbestos corns," especially on left hand and elbow.

Physical signs in chest similar to those in previous case and mainly basal. Clinical findings are those of a bilateral pulmonary fibrosis at both bases with pleural thickening at right base, where on several examinations a pleural rub has been heard.



Drawing of golden yellow asbestos bodies in sputum. 1. (Case II, S.L.) showing dumb-bells about to fracture and produce appearance of clubs. 2. (Case I, C.N.) Dumb-bell-shaped body with central asbestos fibre. 3. (Case I, C.N.) Golden club-shaped bodies in a section of lung asbestosis (post mortem).

Report on X-ray examination of chest (Dr. Stanley Melville).—"Some scoliosis with a dorsal convexity to the left. The heart tends to lie in the hollow of the curve. Restricted movement of the right side of the diaphragm. Right lung: There is evidence of pleural involvement at the base with thickening of the interlobar septum. The basal linear striation is exaggerated, and there is some ill-defined mottling of all zones. Left lung: Some fibrosis at the base. The appearances are compatible with those of an occupational disease."

Sputum examination (Dr. N. H. Schuster).—"A tenacious muco-purulent specimen, with streaks of carbon pigment. Pus cells are numerous. No ciliated columnar cells from the bronchial tract. Many small pointed oval cells, ? fibroblasts. Some large phagocytes. The organisms are numerous and mixed and are mainly *B. friedländer* and pneumococcus. There is also a leptothrix. *B. tuberculosis* not found. Asbestos fibres and 'asbestos bodies' are present." (See fig.)

The presence of "asbestos bodies" in the sputum and the persistent absence of tubercle bacilli together with the clinical and radiological findings, are the factors upon which the diagnosis in these two cases has been made.

These cases are further examples of the harmful effects of asbestos dust, which are due not to free silica, as in silicosis, but to a complex silicate. The relationship

to pulmonary tuberculosis is of great interest. In silicosis tuberculosis almost invariably complicates the position, but it is unusual to find tuberculosis ensuing upon a case of pulmonary asbestosis. I have only one case of the co-existence of pulmonary asbestosis and pulmonary tuberculosis. The fibrosis in pulmonary asbestosis is of a fine diffuse nature, unlike the coarser nodular fibrosis in silicosis.

The onset of symptoms of progressive cough and dyspnœa only after several years' exposure to the dust (average seven to ten years) is interesting. The situation of the lesion—invariably a fine basal fibrosis tending to spread to the middle and finally to the upper zones—is noteworthy. The mechanical effects are greater in this condition than in silicosis owing to the more diffuse fibrosis. The occurrence of repeated colds and acute respiratory infections in these cases was noteworthy. The condition tends to become progressive and the cause of death is, as a rule, an acute bronchopneumonia. Professor Stewart points out that the mere presence of asbestos bodies without clinical and radiological evidence of pulmonary fibrosis does not justify a diagnosis of pulmonary asbestosis. These asbestos bodies are of a golden yellow variety, and are like dumb-bells and clubs in shape. The clubs appear to be fractured "dumb-bells" and they are of coccal and spore-like forms. They usually contain a central translucent asbestos fibre. Dr. R. Gloyne has recently found these bodies in the fæces.

Method of examination of sputum for asbestos bodies.—Dr. Norah Schuster, who has examined a number of specimens for me, employs the following simple method: Mix the sputum with an equal quantity of 4% sodium hydroxide and leave in the incubator until the mucus is dissolved (about one hour usually). Centrifuge. Make a wet film of the deposit and examine directly without staining.

The explanation of the formation of these bodies has been given thus by W. E. Cooke: The central asbestos fibre upon which colloidal aggregates of blood proteins have been adsorbed is moulded into shape by currents in the bronchi and alveoli. The fine specules of asbestos would appear to act mechanically on the bronchioles and alveoli, causing minute extravasations of whole blood or serous exudate which envelops them.

Professor Stewart has had the opportunity of performing a number of post-mortem examinations on these cases, described in an excellent paper by Merewether.

Quite recently a dog, which had been exposed to the dust for eight years, and was obviously dyspnœic, was lethalled.

The lungs, examined by Dr. Schuster, showed macroscopically definite evidence of chronic pleurisy and fibrosis, and microscopically diffuse fibrosis. Dr. Schuster found asbestos *fibres*—not bodies as in the human lung—in the fibrosed lung sections. Why the fibres instead of the bodies should be found in the dog's lung is not easy to explain.

Asbestos "corns" are very common in these workers. The fibres penetrate the skin of the workers, and, as they put it, "Unless we are sufficiently quick to get out the splinter we get a corn." The pathology of these corns has been investigated by Dr. R. Gloyne. They are apparently hyperkeratoses.

Summing up then we may say:—

(1) Symptoms begin only after some years of exposure to the dust, the degree of fibrosis depending upon the nature of the asbestos fibre used. (Three varieties of asbestos fibre were shown at the meeting, viz.: (*a*) white asbestos, (*b*) blue asbestos, (*c*) amosite).

(2) Asbestos bodies can almost invariably be found in the sputum by the concentrated method outlined and there is no real necessity for lung puncture in order to find them.

(3) The presence of asbestos bodies alone indicates exposure to the dust, but before a diagnosis of pulmonary asbestosis can be made, there should be clinical and radiological evidence of a pulmonary fibrosis.

(4) Tuberculosis does not, as in silicosis, complicate pulmonary asbestosis. The cause of death—the lesion is a progressive one—is usually an acute bronchopneumonia.

(5) In contradistinction to silicosis, in which the fibrosis is coarse and nodular, the fibrosis of pulmonary asbestosis is fine and diffuse.

(6) The symptoms are always worse during the winter months, owing to the frequent occurrence of acute respiratory complications.

(7) Treatment, apart from that of a preventive nature (local exhaust ventilation, etc.) can only be symptomatic.

(8) Factors of outstanding importance are: (i) the length of exposure to the dust; (ii) the degree of fibrosis must depend upon the existence or absence of local exhaust ventilation.

Dr. NORAH SCHUSTER said that one point of interest was the lengthy period during which these bodies continued to appear, even after the patient had been removed from the factory and presumably was no longer breathing the dust. One of the girls shown to-day had left the factory three years, yet her sputum had contained a larger number of asbestos bodies than she had seen in anybody else, and there were numerous fibres, with asbestos bodies coagulated round them. So these bodies were embedded in the lung, and their excretion continued a long time after the cessation of exposure to the dust.

She had not yet completed her study of the lungs of the dog referred to, but there were no "bodies" in them. The Prussian-blue test showed no iron-containing colloid in the lungs, but it was full of fibres which were embedded in bronchi and were projecting into the alveolar space. She also found them in the bronchial glands, so evidently there was a circulation of these fibres going on.

General Enlargement of Lymph Glands; Splenomegaly, Enlargement of Head with Œdema of Face.—GEOFFREY L. S. KONSTAM, M.D.

R. G., male, aged 3 years and 3 months. Full term birth; natural delivery; weight 8½ lb. Breast-fed. The head seemed large, and when he was six weeks old swellings were noticed below the chin and in the groins. Backward in walking, but mental development was normal. When aged nine months and a half was admitted to the Hospital for Sick Children, Great Ormond Street, where a tentative diagnosis of generalized glandular tuberculosis was made, based on a biopsy report on an excised gland. Wassermann reaction was negative.

After discharge swellings seemed to grow smaller, but abdomen began to enlarge. A year ago eyelids and face became swollen and glandular masses increased rapidly in size. For six weeks urgently ill with dyspnœa. Dyspnœa is now slightly less marked, but in other respects condition has remained stationary.

On examination.—Dyspnœic, pallid child. Great œdema of face, eyelids (right greater than left) and neck. (See fig.) Enlarged venules right cheek. Circumference of head 21½ in. (normal for child of same age, 19¼ in.). Fontanelle closed. Great enlargement of submaxillary, supraclavicular and axillary glands. These are for the most part discrete, firm, painless and not adherent to deep structures. Glands vary in size from that of a pea to that of an almond.

Pulse regular, 120. Heart normal in size and position; systolic murmur heard at base and apex. Respirations 30, noisy; many rhonchi heard over both sides of the chest. Abdomen greatly distended; small amount of ascites present. Lower pole of spleen one finger's breadth below costal margin. Lower border of liver level of umbilicus; small umbilical hernia present. Fundi, normal. Urine: Trace of protein as globulin and mucin. No Bence-Jones protein present.

A notchy pyrexia (maximum 101·5°) has been present during five weeks' observation in hospital.

Skiagrams (Dr. H. M. Worth).—Skull: Woolly appearance; calvarium thicker than normal. Tibiæ and ribs and distal ends of humeri small, well-defined areas of bone destruction. Femora: wider than normal. Chest: dense shadow to right of mediastinum extending beyond right border of heart.

Wassermann and Kahn reactions negative (23.12.30).

Blood-urea 0·044%. Serum calcium 11·3 mgm. per 100 c.c., serum phosphorus 3·57 mgm. per 100 c.c. Blood cholesterol 190 mgm. per 100 c.c.

Blood-count.—R.B.C.s 3,250,000; Hb. 28%; C.I. 0·43; W.B.C.s 5,600. *Differential.*—Neutros. 52%; lymphos. 48%. The red blood-corpuscles are small and irregularly shaped. No nucleated red cells were found. Diffuse polychromasia. Platelets 200,000.

Report on gland excised from right axilla. (Dr. Elworthy.)—Cut surface red. Microscopy: Subacute inflammatory changes with endothelial cell proliferation. In places

R. G., aged 3¼ years. Photograph shows the enlargement of the head and gross œdema of the face and eyelids.

there is a tendency to necrobiosis. Some of the vessels show endarteritis and periarteritis. There is nothing definitely suggestive of a tuberculous process or of lymphadenoma.

Section stained by Loyez's method was negative for lipins.

Treatment.—Deep X-ray therapy has so far produced no improvement.

Dr. PARKES WEBER said the diagnosis in Dr. Konstam's case seemed to lie between an atypical form of myelomatosis and some hitherto undescribed disease. Yet, one might remember the clear spots shown by radiograms, chiefly in the small bones of the hands, in cases of so-called "benign" lymphogranulomatosis (Schaumann, *Brit. Journ. Derm. and Syph.*, 1924, xxxvi, p. 515).

Tumour of Neck, (?) Carotid Body Tumour. Case for Diagnosis.—S. I. LEVY, F.R.C.S.

E. L., male, aged 48. Painless swelling in the right side of the neck appeared six years ago. Patient seen at another London hospital, where swelling was thought to be glandular and secondary to infected tonsils. Tonsillectomy advised and performed, but no alteration in size of swelling noticed. Subsequently the teeth were incriminated and extracted. Mass remains painless and stationary in size, with no change during ingestion of food. It appears to be solid; it is situated opposite the level of the greater cornua of the hyoid bone, which can be felt over it, and pulsation of carotid vessels is transmitted through it. The tumour can be felt pushing into the right lateral pharyngeal wall; pharyngeal and laryngeal examination otherwise negative. Patient appears to be able to dislocate pharynx and larynx to affected side and thus makes tumour more prominent.

Skiagram of neck shows nothing abnormal. Wassermann reaction, negative. Blood-count normal.

Specimen Showing Scar of what had been a Large Gastric Ulcer Healed under Medical Treatment a Year Previously.—TERENCE EAST, M.D.

This is a specimen of stomach with a small scar, almost invisible, on the lesser curvature. This scar had been the site of a large ulcer, which was demonstrated in a skiagram taken after a barium meal a year before death. The ulcer healed under medical treatment—the patient died a year later as the result of a coronary thrombosis.

Banti's Disease with Rheumatic Endocarditis.—H. V. MORLOCK, M.D.

Male, aged 22. Admitted to hospital complaining of dyspnœa. Has lived a normally active life until five years ago, when he had a copious hæmatemesis and was in hospital for five months. Two years ago had œdema of legs, which disappearad after two weeks' rest in bed; since then has felt quite well, apart from dyspnœa on exertion.

Past history.—Thirteen years ago was known to have large liver and spleen.

Condition on examination.—Frail, undersized youth. Pale, slight icteric tinge.

Heart: Apex beat just outside nipple line in fifth space; mitral presystolic and systolic murmur; aortic diastolic murmur.

Abdomen: Spleen enlarged to two inches and a half below umbilicus. Surface smooth. Liver easily felt on inspiration: firm, surface uneven. No ascites. Nothing else abnormal discovered.

Blood-count.—R.B.C.s 4,900,000; Hb. 42%; C.I. 0·43; W.B.C.s 5,600. *Differential.*—Polys. 76·7%; eosinos. 1·6%; large monos. 3·5%; lymphos. 16·7%, myelos. 1·4%; blood-platelets 250,000.

Van den Bergh reaction.—Direct: Very weak, delayed; indirect: 1·5 units.

Bleeding time.—Patient, 3 min. 10 sec. Control, 2 min. 50 sec.

Fragility test.—Patient: Hæmolysis begins in 0·45% saline and is complete in 0·35%. Control: Hæmolysis begins in 0·45% saline and is complete in 0·35%.

Blood Wassermann reaction.—Negative.

Fractional test meal.—Resting juice was bile-stained and contained no charcoal. Curve of acid secretion lies towards the lower normal limit. Emptying of stomach is delayed since starch is present for 2½ hours. Bile is present in several specimens.

Epithelioma of the Larynx. Relief of pain by alcohol injection of the superior laryngeal nerve.—SIR JAMES DUNDAS-GRANT, K.B.E., M.D.

A man aged 62 with symptoms of carcinoma of the larynx, when seen in July 1930 complained of pain and hoarseness, preceded by discomfort in the throat for 12

months, and a hard fixed glandular enlargement on right side of the neck. In October 1930 had extreme pain on right side of throat. A week later an alcohol injection into the superior laryngeal nerve was made; this was followed by great relief which lasted for six weeks; the pain then returned and the injection was repeated, the pain being relieved up to the present time.

Tuberculosis of the Larynx with pain instantly relieved by galvano-cautery.—Sir JAMES DUNDAS-GRANT, K.B.E., M.D.

Patient, a man in early middle life. When first seen the epiglottis was extremely infiltrated throughout, and there was a small outgrowth at middle of its tip. Pain on swallowing was intense. Epiglottis was subjected to galvano-caustic puncture in three places. At present there is considerable infiltration and irregular shrivelling. The patient is in perfect health and is profuse in his expression of the relief from pain he experienced immediately after the cauterization.

Section of Medicine.

[Cases shown at a Meeting held at Guy's Hospital, November 25, 1930.][1]

By A. F. Hurst, M.D., and C. F. Cosin, M.B.

Hyperparathyroidism with Hypercalcæmia and Decalcification of Bones.—The patient was a boy, aged 17, from whom a cystic parathyroid adenoma had been excised by Mr. Slesinger.

Two Cases of Anæmia following Gastro-Enterostomy for Duodenal Ulcer.—In the first case the anæmia was of the microcytic type and had responded to treatment by iron; in the second it was of the megalocytic type and had responded to treatment by liver. In both a test-meal before the operation had shown a normal acid curve and after the operation complete achlorhydria.

Aplastic Anæmia in a Man, aged 33.—The patient had received over a hundred transfusions in a period of five years. The blood throughout had shown a slight eosinophilia, and a piece of bone-marrow, removed at biopsy, showed excess of eosinophil-myelocytes. No parasites of any kind had been found, and all investigations as to the cause of the anæmia proved negative. Neither iron nor liver and stomach had any effect. The hæmoglobin, which is now 80%, has been as low as 25%.

By J. J. Conybeare, M.D.

Diaphragmatic Hernia with Displacement of Liver and Cirrhosis, in a Girl aged 12.—X-ray examination showed that the stomach lay entirely on the left side of the abdomen. The whole of the small intestine, cæcum, ascending colon and transverse colon lay above the liver, occupying the lower part of the thoracic cavity. The outline of the left diaphragm could be seen, and the intestine appeared to lie above it. On the right side the intestines appeared to lie below a much elevated diaphragm.

By L. J. Witts, M.D.

Two Cases of Splenomegalic Polycythæmia.—In one, the platelet count was 900,000 and the patient had recently had an attack of ascites from which he had recovered on treatment with a salt-free diet, ammonium chloride and novarsurol. It was suggested that the portal vein had become thrombosed.

In the second case, the index finger of the right hand had been amputated on account of gangrene. The red cells, which had been 8,500,000, had fallen to 4,800,000 on treatment by deep X-rays. The general condition had greatly improved.

Three Cases of Hepatic Cirrhosis with Diabetes Mellitus.—The first patient, a man aged 59, had been admitted to hospital after hæmatemesis of about one pint. He was very obese and the fasting blood-sugar was 0·25%. The diabetes was controlled by diet alone.

The second patient, a man, aged 46, was suffering from relatively acute diabetes. The skin was rather grey and pigmented, and the liver was palpable. He had kept well on a diet of 1,750 calories and insulin 20 units b.d.

The third patient was a woman, aged 59, who had been admitted to hospital eighteen months previously on account of jaundice, thirst and epigastric pain. The liver and spleen were both enlarged 2 in. below the ribs. There was glycosuria,

[1] The publication of this report was deferred, as it was insufficient in itself to constitute a fasciculus.—[Ed.]

and the blood-sugar was 0·4%. The stools contained a large excess of fatty acid crystals.

Dr. F. PARKES WEBER said that in the second case the condition was certainly hæmochromatosis, but in some cases visceral hæmochromatosis was present without any cutaneous pigmentation.

By E. P. POULTON, M.D.

Infectious Jaundice and Epididymitis.—The patient, a man aged 58, had been gravely ill with febrile jaundice. There was also herpes labialis and the urine contained *B. coli*. Investigations for spirochætes were negative. The jaundice had gradually remitted and the temperature settled in four weeks, then suddenly rose to 104° with the onset of epididymo-orchitis. The temperature fell to normal again in a week, the epididymitis improving. It was suggested that both the jaundice and the epididymitis were the result of *B. coli* infection. Gall-stones were excluded.

By R. S. BRUCE-PEARSON, L.R.C.P. and S.Ed.

Milroy's Disease.—The patient was a woman whose mother and brother had also been affected.

Discussion.—Dr. E. P. POULTON advised treatment with large doses of thyroid. [Dr. BRUCE-PEARSON said this had already been tried with no good effect.]

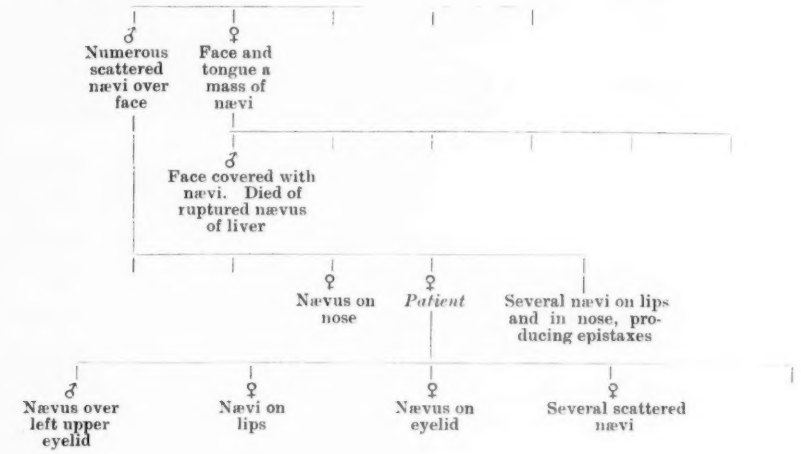
Dr. PARKES WEBER said that in Milroy's disease ("trophœdema," &c.) the distribution of the swelling in the limbs varied greatly in different cases, even in different members of the same family group. He thought, therefore, that the cause of the condition must be some undiscovered local congenital-developmental structural abnormality affecting the lymphatic circulation in the swollen extremities and was not due (as some had suggested) to a general endocrine (thyroidal secretion) abnormality.

By R. E. SMITH, M.R.C.P.

(1) Hodgkin's Disease treated by Radium; (2) Anterior Poliomyelitis, affecting the Right Shoulder-girdle; (3) Aortic Stenosis.

By A. C. HAMPSON, M.C., M.D.

Three Cases of Congenital Telangiectasis.—In all three cases there was a family history of the same complaint, as is illustrated by the following table from one of the cases.


♂ Numerous scattered nævi over face
♀ Face and tongue a mass of nævi
♂ Face covered with nævi. Died of ruptured nævus of liver
♀ Nævus on nose
♀ *Patient*
Several nævi on lips and in nose, producing epistaxes
♂ Nævus over left upper eyelid
♀ Nævi on lips
♀ Nævus on eyelid
♀ Several scattered nævi

Dr. PARKES WEBER said that he would include all these cases, together with certain other cases of hæmoptysis, gastrostaxis and "telangiectatic hæmaturia," in a group which he would term *congenital-developmental telangiectasia, familial or non-familial, often with hæmorrhagic tendency.* In a paper in the *British Journal of Children's Diseases* (1924, xxi, 198-202) he had endeavoured to extend Osler's original group of cases in that way. Even so enlarged, the group constituted only a part of a larger group of congenital-developmental abnormalities of blood-vessels (embracing racemose angiomata, cavernomata and hæmangio-endotheliomata or hæmangioblastomata).

By L. J. WITTS, M.D., and E. T. CONYBEARE, M.D.

Familial Essential Thrombocytopenia in a boy aged 7, who had suffered from bleeding from the gums and excessive bruising since the age of four.

Blood-count.—R.B.C.'s 4,950,000, W.B.C.'s 7,900, Hb. 65%, platelets 40,000, bleeding time 10 minutes, coagulation normal. Spleen not enlarged.

Family history.—His brother, aged 20, was under treatment here for the same condition, which had been present since aged 5. His platelets fluctuated between 20,000 and 100,000; spleen not enlarged. There was no response to treatment by liver, and he died after splenectomy. A sister died, aged 5, from epistaxis. The parents (who are not cousins) and two other children are alive and well. It has been possible to examine only the mother; her blood is normal.

Dr. J. M. H. CAMPBELL showed Electro-cardiograms of Cases of Heart-block.

Dr. F. A. KNOTT showed Blood Films of Acute and Chronic Leukæmia, and the Preparations illustrating the Phagocytic Test used in the Control of X-ray Treatment.

[*January* 27, 1931.]

Heart Disease Complicating Pregnancy.

By CRIGHTON BRAMWELL, M.D.

(I) INTRODUCTION.

(*a*) *Prognosis of heart disease in pregnancy.*—I have selected this subject because it is one in which I am particularly interested at the moment, and one concerning which the information in many current textbooks is neither adequate nor up to date. The reason for this is that the obstetrician cannot be expected to keep pace with each new advance in cardiology, whilst the cardiologist rarely has the opportunity of making really satisfactory observations on this subject. He is called in consultation to express an opinion on prognosis, or to give advice on treatment, but he does not generally have the chance of supervising that treatment himself or of watching its results. Nor does he always hear whether his prognosis proved correct, or otherwise, and there is nothing more fatal to progress than ignorance of one's mistakes.

When a patient suffering from heart disease becomes pregnant the question may arise as to whether the pregnancy should be allowed to pursue its normal course. The answer to that question must depend essentially on two considerations: (1) What is the *immediate risk*, to the mother, of pregnancy and labour? (I mean the additional risk imposed by the presence of heart disease); (2) To what extent are pregnancy and labour likely to impair the patient's future health by producing a *permanent aggravation* of the cardiac disability?

If, in any given case, one decides that pregnancy should be terminated prematurely, the further problem arises: (3) When and how should this be done?

To attempt to answer these three questions is the object of my paper.

During the past three years, Dr. Norah Regan and I have made a careful study of cardiac cases attending the ante-natal clinic, or admitted to the wards, of St. Mary's Hospital in Manchester. We have kept in touch with these patients and watched their symptoms throughout the later weeks of pregnancy, through labour and the puerperium, to see how the damaged heart stood the additional burden which it was called upon to bear. And finally, we have re-examined most of them some months after confinement, in order to ascertain whether the heart appeared to have suffered any further permanent damage as the result of pregnancy and labour.

(*b*) *Material.*—The clinical material in this investigation consists of two series of cases. The first series, comprising 82 patients, includes all grades of heart disease, from the most severe to the most trivial. It is a consecutive series of unselected cases. By that I mean that it includes every case of pregnancy seen at St. Mary's Hospital, during a period of about 18 months, in which heart disease was detected. Three of these patients were admitted directly to the wards on account of heart disease, the other 79 cases were drawn from 3,185 women examined by Dr. Regan at the ante-natal clinic.

The second series differs from the first in that it is not consecutive. It was recruited from patients in whom heart disease was diagnosed or suspected in the first instance, not by us, but by some member of the honorary or resident obstetric staff of the hospital. These patients were referred to us for diagnosis and medical treatment.

In 26 cases in this series we found evidence of an organic heart lesion.

I shall confine my attention almost exclusively to the first series, since it constitutes a fairer sample of the incidence of heart disease in the working-class population of an industrial area, and being a consecutive series of unselected cases, it fulfils more nearly what scientifically one might call a "clean" experiment.

(*c*) *Method of investigation.*—For the purpose of this investigation I drew up a special case sheet (figs. 1-4).

(*A*) History.—Section A is self-explanatory. The first two paragraphs—the "Obstetric History" and "First Obstetric Examination"—are completed at the time the patient is first seen, whether at the ante-natal clinic or in the ward. She is then brought up to my out-patient clinic at the Royal Infirmary for the completion of Section D. A full medical history is taken, and she is closely questioned regarding the various types of rheumatic infection and other illnesses likely to have been responsible for initiating or aggravating the cardiac lesion.

(*B*) Physical Examination.—In Section D II are enumerated the physical features which I consider to be the most important in the examination of a case of chronic heart disease.

(1) Congestive heart failure. Of these the first is evidence of venous congestion, as manifested by engorgement of the veins of the neck, enlargement of the liver, moist sound at the bases of the lungs, and œdema.

(2) Cardiac enlargement. In addition to palpation of the maximal cardiac impulse and percussion as a means of determining the size of the heart, a six-foot X-ray film has been taken in each case. For this we are indebted to our colleagues Dr. R. S. Paterson and Dr. E. W. Twining, of the Manchester Royal Infirmary.

(3) Disorders of rhythm. An electrocardiographic examination was made in each case in addition to the usual routine clinical examination.

(4) Valvular lesions. I have placed these last on the list intentionally, because when regarded from the point of view of prognosis, they afford less valuable information than any of the other three features. Valvular lesions belong to the field of diagnosis, and here we are concerned primarily with prognosis. The same applies to those auscultatory signs which afford evidence of congenital heart lesions. In these also it is the associated cardiac

No.....

N.B.—1. When space provided in this form is insufficient, further notes may be made on the blank pages 5 and 6.

2. This form is to be returned to Dr. Bramwell when the Patient is discharged from Hospital.

ST. MARY'S HOSPITAL.

CARDIAC CASE SHEET.

Name..... *Hospital No*.....

Address .....

Surgeon..... *Age*..... *Occupation*.....

G.P......

Admitted I.P...... *Discharged*.....

Result.....

A.—OBSTETRIC HISTORY AND EXAMINATION.

I HISTORY.

PREVIOUS LABOURS.

a. Date				
b. Prematurity				
c. Mode of delivery				
d. Duration of labour				
e. Weight of child				
f. Puerperium				
g Remarks				

ABORTIONS.

Wassermann Reaction.....

II. FIRST OBSTETRIC EXAMINATION. *Date* _____

a. First day of last m.p ..... 36th week _____

b. Pelvic measurements (if abnormal) _____

c. Presentation and position ..... _____

d. Urine..... Sp.G. _____ Alb. _____ Sug. _____

e Other abnormal features ..... _____

Obstetrician's Signature _____

III OBSTETRIC EXAMINATION 36TH WEEK. *Date* _____

a Disproportion, etc ..... _____

b. Urine..... Sp G _____ Alb _____ Sug. _____

c. Other abnormal features ..... _____

Obstetrician's Signature _____

FIG. 1.

B.—LABOUR. *Date*.....

Period of Gestation..... *Weight of Child*.....

	Time.	Pulse.	Abnormal features (cyanosis, dyspnoea, collapse, etc.)	Inertia.
Onset, 1st stage				
Rupt. of memb.				
Onset, 2nd stage				Loss (normal, excessive).
Delivery of child				
Delivery of Placenta				

Mode of Delivery: (*a*) Child (*b*) Placenta

Anæsthesia or narcosis

Remarks

Obstetrician's Signature.....

C.—PUERPERIUM.

Method of Feeding.....

Date.															
Pulse.	Temp.														
x	o														
140	105														
130	104														
120	103														
110	102														
100	101														
90	100														
80	99														
70	98														
60	97														
Urine (Albumin)															
Resp.															
Bowels.															

FIG. 2.

D.—CARDIAC HISTORY AND EXAMINATION.

I.—HISTORY.

1. AETIOLOGY, R.F.
   Chorea
   Tonsilitis
   Other Illnesses

2. SYMPTOMS (oedema, dyspnoea, fatigue, palpitation, etc.)

(*a*) During present pregnancy

(*b*) Prior to present pregnancy—Exercise Tolerance.

(*c*) During previous pregnancies

II.—EXAMINATION. *Date*.....

Congestion	Neck Liver Lungs	Oedema Cyanosis Pallor	
Enlargement		M.I. on back character	on L side M.C.L.
Rhythm		Pulse resting rate character B.P.	
Valves		Heart Sounds	
X-Ray			
E.C.G.			
Remarks			

PROGNOSIS

Cardiologist's Signature.....

FIG. 3.

E.—SUBSEQUENT CARDIAC EXAMINATIONS DURING PREGNANCY.

Date	
Dyspnœa	
Oedema	
Congestion	
Impulse	
Pulse	
B.P	
Urine	

F.—CARDIAC EXAMINATION DURING PUERPERIUM. *Date*.....

Symptoms since delivery

Physical Examination

Remarks

G.—FINAL STATE. *Date*.....

Symptoms

Physical Examination

Remarks

H.—SUMMARY OF CASE.

FIG. 4.

enlargement and disturbance of the heart's function, as manifested by venous engorgement, and by disorders of rhythm, on which we must rely in framing our prognosis.

(*C*) Progress.—During the later part of pregnancy the patients came up for re-examination at fortnightly intervals, and the further progress of the case, with any new developments, was noted in Section E. The duration of labour and any complications were recorded in Section B. Those patients who were confined in St. Mary's Hospital were seen by one of us during the puerperium, and their condition summarized in Section F. Patients were requested to report at the Royal Infirmary one month after confinement and subsequently at intervals of three months. Those who failed to do so were visited in their homes, but 12 patients have been lost sight of owing to change of address.

(II) Results of Investigation.

(*a*) Ætiology.—Sixteen patients gave a history of rheumatic fever alone, 11 gave a history of chorea, while 10 had suffered from both diseases. In addition recurrences were noted in 14 cases. Six patients had had two attacks and one patient had had three attacks of rheumatic fever. Four patients had had two attacks of rheumatic fever in addition to chorea, one had rheumatic fever and two attacks of chorea, while one had suffered from rheumatic fever three times and chorea once. Three others gave a history of more than one attack of chorea uncomplicated by rheumatic fever. Eleven who had never had either typical rheumatic fever or chorea admitted to having suffered from "rheumatism," while six who had had chorea and four who had had rheumatic fever in childhood subsequently suffered from "rheumatism."

Twenty who were found on examination to have mitral stenosis had no recollection of having suffered at any time from either rheumatic fever, chorea, or rheumatism. Eleven of these, however, had had either growing pains or tonsillitis, and there can be little room for doubt that the cardiac lesion was of rheumatic origin.

Apart from the 20 patients with mitral stenosis, there were four who gave no rheumatic history. Of these, three had congenital heart lesions and one had an enlarged heart without any valvular lesion.

(*b*) Symptoms. *Dyspnœa and œdema.*—Of the 82 cases, 36 were primiparæ and 46 multiparæ. Of the multiparæ 11 were first seen during their second pregnancy, 12 during the third, 10 during the fourth, 10 during the fifth, and one each during the seventh, eighth and fourteenth pregnancies. All the primiparæ had cardiac symptoms during pregnancy, and 21 also gave a history of dyspnœa or palpitation prior to pregnancy, but only three had noticed œdema previously, whereas 12 observed œdema for the first time during pregnancy. Of the 46 multiparæ, 18 had dyspnœa or palpitation and three had œdema prior to pregnancy, whilst 16 noticed œdema for the first time during the current pregnancy.

We may therefore classify our patients into three groups: (1) The trivial cases —in which there are no symptoms of circulatory insufficiency, even during pregnancy. In this group there were only four patients in the present series. They were all multiparæ with uncomplicated rheumatic mitral stenosis.

(2) The early cases—in which the patient had been unaware of any cardiac disability until she became pregnant, having previously been able to undertake her ordinary household duties without any signs of circulatory insufficiency. There were 12 primiparæ and 21 multiparæ in this group.

The multiparæ in this group may be further subdivided into: (*a*) those in whom symptoms of circulatory insufficiency appeared for the first time during the present pregnancy, and (*b*) those in whom the symptoms had been present during previous pregnancies but had disappeared in the interval between successive pregnancies. In the second group we must ascertain whether the symptoms during

the current pregnancy have been more severe than was the case at corresponding stages of previous pregnancies (i.e. whether there is any evidence that the cardiac lesion has progressed).

(3) The more advanced cases—in which the patient has been aware of some degree of limitation of the cardiac reserve prior to pregnancy. There were 24 primiparæ and 21 multiparæ in this group.

Apart from dyspnœa and œdema, the only symptoms to which I wish to refer are cough and hæmoptysis.

Cough.—Chronic bronchitis was present in 11 cases. In four of these it had only appeared during the later half of pregnancy, but in the other seven it had been present for several years. In three of the latter there was no doubt that the cardiac condition was definitely aggravated by the bronchitis. All three were admitted to hospital for treatment, and one has remained in poor health since confinement. In her case, however, in addition to mitral stenosis, there was aortic incompetence and stenosis, and one is bound to regard the cardiac lesion as an important factor in the development of congestive heart failure.

Hæmoptysis.—This symptom was complained of by only five patients during pregnancy, all of whom had mitral stenosis, complicated in two cases by aortic regurgitation (Cases 4 and 65). In Case 65 the hæmoptysis was copious, while in Case 4 it had occurred for a week following the last confinement. In another (Case 35) it commenced during the fourth month and was of frequent occurrence. Hæmoptysis was much less common in our series than in that recorded by Hay and Hunt [1], who noted a peculiar liability to this symptom in pregnant women with heart disease, recording its occurrence in 30 per cent. of their cases.

(*c*) VALVULAR LESIONS. (Table I).—Sixty-seven of the 82 patients in our series had mitral stenosis. Of these, seven also had aortic incompetence. Two of the cases with aortic incompetence also had aortic stenosis. Both of these, as well as the patient with tricuspid incompetence, developed congestive heart failure and have been in poor health since confinement. These three cases are described more fully below.

Mitral stenosis.—Since this lesion was present in 67 of the 82 cases in the present series, it may be regarded as the usual valvular lesion to which the conclusions of the investigation as a whole apply. For the moment, therefore, I shall deal only with those cases in which mitral stenosis was not present, or was complicated by some other valvular lesion.

TABLE I.—VALVULAR LESIONS.

Mitral stenosis	59	
Aortic incompetence	5	
Aortic incompetence and stenosis ...	2	
Tricuspid incompetence	1	67
Mitral incompetence		10
Congenital:		
Patent ductus	2	
Pulmonary stenosis	1	3
No valvular lesion		2
Total		82

Mitral incompetence.—In 10 cases in which there was a definite rheumatic history and an apical systolic murmur, but no definite evidence of mitral stenosis, mitral regurgitation was diagnosed. In all these cases a presystolic murmur was sought for with the patient lying on the left side as well as on the back, both before and after exercise. One of these (Case 7) had a high blood-pressure (150/85) and developed symptoms of renal toxæmia. She was delivered prematurely at the thirty-second week. Another gave 19 years' history of dyspnœa and had been subject to œdema of the ankles prior to pregnancy. She was delivered prematurely at the thirty-ninth week. Another was induced at the fortieth week for post-maturity. Seven cases in this group were delivered at full term.

Aortic incompetence.—It is customary and natural to regard the additional lesion of aortic incompetence in patients with rheumatic mitral stenosis as a factor adding to the gravity of the prognosis. This, however, is not borne out by the cases in our series (Table II). None of our five fatal cases had aortic incompetence, and of the seven cases in which this lesion was present, two only caused us any anxiety. Both of these patients had aortic stenosis in addition to incompetence, both were women over 30 years of age, in their fifth pregnancy, and both exhibited evidence of an advanced degree of congestive heart failure. In one of these patients (Case 4) the cardiac condition was undoubtedly aggravated by the presence of severe bronchitis. while the other (Case 73) had suffered from dyspnœa on exertion for 20 years. Of the remaining five cases with aortic incompetence none gave any trouble. In one primipara (Case 67) labour was induced at the thirty-ninth week on account of pelvic contraction. In another primipara (Case 65) labour was induced on account of hæmoptysis.

Two patients had cardiac enlargement without any evidence of valvular disease and three had congenital heart lesions. None of these gave any trouble.

TABLE II.—AORTIC LESIONS.

Case	Para	Age	Lesion	Size	B.P.	Labour	Result
4	5	32	I.S.	15·6	110 60	Premature 39	Ill, C.H.F.
31	3	23	I.	15·8	140 60	Premature 36	
37	3	22	I.	15·0	130 60	Premature 36	
73	5	38	I.S.	16·0	145 70	Induced 36	Ill, C.H.F.
80	5	31	I.	15·1	145 55	Full-term natural	
65	1	21	I.		120 50	Induced 38	
67	1	24	I.		130 80	Induced 39 (constricted pelvis)	

I. = Incompetence. I.S. = Incompetence and stenosis. C.H.F. = Congestive heart failure.

(*d*) BLOOD-PRESSURE.—The question of the effect of pregnancy on the blood-pressure has been studied by several workers.

In our series the average systolic blood-pressure was between 110 and 120, and the diastolic between 70 and 80. In the last few weeks of pregnancy a slight increase occurred in the majority of cases and persisted during the puerperium.

The systolic blood-pressure was 140, or over, in 11 cases in this series. Of these three had aortic incompetence (Cases 31, 73 and 80), and two (Cases 7 and 70) developed signs of renal insufficiency. In two (Cases 5 and 8) there was no valvular lesion, but the heart was enlarged. The other four were all primiparæ, who presented no features of special interest.

(*e*) CONGESTIVE HEART FAILURE.—Six patients in this series had signs of congestive heart failure (Table III). One of these, a primipara (Case 60), had a very large heart and developed auricular fibrillation at the thirtieth week. Labour was induced at the thirty-sixth week and the patient died two weeks later from septic complications. Another (Case 83), who was admitted to hospital as an urgency case and delivered the following day, died six weeks after delivery. Three others (Cases 4, 61 and 73) have been in poor health since confinement. Although these three were all multiparæ their cardiac condition appears to have been definitely aggravated by the current pregnancy. One patient only out of the five appears to have been none the worse.

The good result in her case may be accounted for by the fact that the heart failure was largely attributable to bronchitis.

TABLE III.—CONGESTIVE HEART FAILURE.

Case	Para	Age	Dyspnœa years	Heart size	Labour	Result	Remarks (all mitral stenosis)
4	5	32	5	15·6	Premature 39	Ill since	Aortic incompetence and stenosis. Bronchitis
61	3	30	12	15·1	,, 36	Ill since	Tricuspid incompetence
73	5	38	20	16·0	Induced 36	Ill since	Aortic incompetence and stenosis
35	1	21	7	15·3	,, 39	Well	Bronchitis
60	1	26	8	18·9	,, 36	Died, sepsis	Auricular fibrillation 30th week
83	1	25	(20)	no X-ray	Premature 32	Died, pulmonary œdema	

It is noteworthy that only one of these six patients had auricular fibrillation, in the other five failure was associated with normal rhythm, an unusual condition in rheumatic heart disease.

Three other patients gave a history of having had œdema as well as dyspnœa prior to pregnancy, but only one of them (Case 66), a multipara, aged 30, whose dyspnœa dated from rheumatic fever nineteen years previously had any œdema when under our care. Symptoms in another case dated from rheumatic fever seven years previously. Both of these patients were slightly premature, but in all other respects labour was normal, and no complications occurred subsequently. The remaining patient (Case 81) in this group was a primipara, aged 21, whose condition was complicated by the presence of heart block. She had congestion in the veins of the neck when we first saw her, but no œdema. She went into labour at the thirty-fourth week and died a few hours later.

One would have expected that those patients who gave a history of dyspnœa and œdema prior to pregnancy would have developed signs of venous congestion during pregnancy and vice versa. In our series, however, of the six patients who had congestive heart failure during the pregnancy which we observed, two only gave a history of œdema prior to pregnancy, whereas four others who gave a positive history did not develop congestive heart failure during pregnancy, in spite of the fact that three of them were primiparæ.

These discrepancies are distinctly disconcerting, for one would have expected that the presence or absence of œdema associated with dyspnœa, prior to pregnancy, in patients with rheumatic heart disease, would have proved to be a criterion to which we could have attached considerable importance in prognosis. This expectation has not been justified. It may be that the clinical histories are unreliable. The memories of some patients are short-lived, and it may require a prolonged cross-examination to elicit the facts of the case. At the time these histories were taken we were content to accept the patients' statement that their feet had not been swollen, and we did not pursue the inquiry farther, as perhaps we should have done. We are now endeavouring to ascertain whether this explanation is correct, by more careful questioning.

A possible explanation of the absence of congestive heart failure in patients who give a history of œdema prior to pregnancy is that the œdema was not of cardiac origin.

(*f*) AURICULAR FIBRILLATION.—Auricular fibrillation was present in only three patients in this series. One was a primipara (Case 60) in whom fibrillation appeared at the thirtieth week of pregnancy. She had all the signs of congestive heart failure and her heart was greatly dilated. She died from septic complications two weeks after delivery.

The other two patients were both multiparæ in whom fibrillation was already established when we first saw them.

One (Case 30), a woman, aged 39, in her second pregnancy, had suffered from dyspnœa on exertion ever since rheumatic fever at the age of 8. She had been seen by one of us two years previously during an attack of rheumatic fever with auricular fibrillation, and normal rhythm had been restored with quinidine. Fibrillation recurred and persisted throughout pregnancy, and for twelve months afterwards. The dyspnœa had increased during pregnancy but she had never noticed any swelling of the ankles, and had no signs of heart failure when we saw her. Pregnancy was uneventful and she had a $5\frac{3}{4}$ lb. healthy baby at full term. There was no undue distress during labour, which lasted eight hours. The cardiac condition in this case does not appear to have been detrimentally affected by pregnancy.

The other (Case 82) was a woman aged 39 in her fourteenth pregnancy. She had been short of breath for eight years, but manifested no signs of heart failure. She died two months after confinement, but her death was undoubtedly attributable

to her refusal to follow medical advice or to observe any reasonable precautions. Thus the two cases in this series in which auricular fibrillation was uncomplicated by the presence of heart failure, got through pregnancy and labour without any cardiac complications.

In a series of 18 patients with auricular fibrillation complicating pregnancy reported by Leyland Robinson [2] there were thirteen deaths. One must take into consideration, however, the fact that eight of Robinson's fatal cases did not receive in-patient treatment during the course of pregnancy, though all had congestive heart failure.

(*g*) HEART BLOCK.—Partial heart block was present in one patient (Case 81) in our series. She had an old-standing rheumatic mitral stenosis, and had only been able to work intermittently during the past two years on account of increasing dyspnœa. She had a partial left hemiplegia in February, 1927, another in May, 1928, from which she soon recovered, and a third, involving the left arm and leg, in November, 1928, the effects of which were still present when we first saw her six weeks later.

Towards the end of pregnancy she began to complain of pain under the left breast associated with a sensation of suffocation. During these attacks the pulse became weak, rapid, and irregular, but we did not have the opportunity of taking further electro-cardiograms. On February 2 the heart-rate was 96 and its rhythm regular, and the blood-pressure had fallen from 125/80 to 105/75. The following day she went into labour and died two hours later.

(III) DISCUSSION.

Treatment during pregnancy.—All patients in this series came up for re-examination once a fortnight, during the later months of pregnancy. They were advised to take a light diet, to pay attention to the skin and bowels, and to avoid as far as possible any exertion which provoked dyspnœa or palpitation.

All the primiparæ and those of the multiparæ (with the exception of Case 82) in whom there was reason to anticipate possible cardiac complications were admitted to St. Mary's for confinement.

(*a*) FATAL CASES (Table IV).—Three patients in this series never attended the ante-natal clinic but were admitted directly to the wards—one (Case 60) from the out-patient department, and the other two (Cases 81 and 83) at the request of their own medical attendant. All these patients were dangerously ill at the time of admission and all three died in hospital. One (Case 60) had a very large heart. She developed fibrillation in the thirtieth week and labour was induced six weeks later. After induction a swinging temperature developed, with signs of septic infection, from which the patient died two weeks later.

The second (Case 83) was admitted as an urgency on account of congestive heart failure in the thirty-second week of pregnancy. She was delivered the day following admission and died from acute pulmonary œdema six weeks later.

The third was admitted to hospital on account of embolic hemiplegia with partial heart block. She was delivered prematurely at the thirty-fourth week and died 2½ hours after delivery.

TABLE IV.—FATAL CASES.

Case	Para	Age	Labour		Date	Cause	Admitted for	Remarks
21	1	28	Induced ...	39	3 days	Pulmonary embolism	Hæmoptysis	
60	1	26	,, ...	36	2 weeks	Sepsis	C.H.F.	Auricular fibrillation 30th week, heart 18·9 c.m.
83	1	25	Premature...	32	6 weeks	Pulmonary œdema	C.H.F.	
81	1	21	,, ..	34	2½ hrs.	Periph. failure	Hemiplegia	Heart block
82	14	39	Full-term natural		2 mths.	Refused treatment	Auricular fibrillation	Auricular fibrillation

C.H.F. = Congestive heart failure.

One of the other two fatal cases was the woman to whom I have already referred (Case 82), who died two months after confinement as the result of deliberate neglect of reasonable precautions. In the remaining case, the patient was a primipara, aged 28, who was admitted to hospital on account of hæmoptysis and died from pulmonary embolism three days after confinement.

(*b*) UNFAVOURABLE RESULTS.—In addition to the five fatal cases enumerated above there were three patients whose cardiac condition appeared to be definitely aggravated by the pregnancy in question.

All three were multiparæ over 30 years of age, who had complained of dyspnœa for some years previously, and two in addition had had œdema. All three were admitted to hospital for treatment during the later stages of pregnancy on account of congestive heart failure. They responded well to rest and digitalis. In addition to cardiac enlargement and mitral stenosis two had aortic incompetence and stenosis, and one had tricuspid incompetence. Labour occurred prematurely (at the thirty-sixth and thirty-eighth week) in two cases, while the third was induced at the thirty-ninth week. In her case only was there any distress during labour.

In only five other cases in this series did we consider it necessary to admit the patients to hospital for treatment previous to labour. One of them, a primigravida, aged 21, who gave no rheumatic history, but had mitral stenosis and had suffered from dyspnœa on exertion since the age of 14. She was induced at the thirty-ninth week and manifested some distress during confinement. This was the only case in our series with pronounced cardiac muscle failure which did well, and the favourable result in her case is probably explained by the fact that the heart failure was largely attributable to a severe attack of bronchitis.

The other three cases were all admitted to hospital on account of increasing dyspnœa, which in one case was partly attributable to bronchitis.

(*c*) PARTURITION.—Delivery has been effected in all of the 83 cases in the series, 63 cases in St. Mary's Hospital, 14 at home, and six in the Union Hospital.

Date and method of delivery (Table V).

(1) *Labour at full term.*—Labour occurred at full term in 44 cases, 20 were primigravidæ and 24 were multigravidæ. All of the multigravidæ were delivered by natural forces, without any distress, the average duration of labour being nine hours seven minutes, and all had living children.

Of the primigravidæ, 18 were delivered by natural forces without distress. The remaining two had some distress, with dyspnœa and rapid pulse during the second stage; low forceps were applied and extraction effected. The average duration of labour was 17 hours 15 minutes[1]; the longest time being 61 hours 30 minutes (Case 46).

TABLE V.—PARTURITION.

		Primiparæ	Multiparæ
43	Full term	19	24
25	*Premature*—		
	37 to 39th week ...	6	11
	prior to 37th week ...	2	6
12	*Induction*—		
	for pelvic contraction ...	4	—
	for post-maturity ...	1	2
	for cardiac condition ...	4	1
2	Cæsarean section ...	—	2
82			

All of the primigravidæ had living children.

In this series 42 of the 44 cases passed through a normal delivery without any undue distress. With each pain the pulse-rate increases and the blood-pressure

[1] The figures are only approximate, as in some cases the house surgeon in charge of the case omitted to record the necessary data.

rises, but the condition of the pulse between the pains is a guide to the response of the heart to the increased work caused by labour. There was no undue acceleration of the pulse-rate during labour except in the two primigravidæ noted above.

(2) *Premature labour.*—Delivery occurred before full term (as calculated from the first day of the last menstrual period) in 25 cases. Eight of these were primiparæ, all of whom were delivered by natural forces. Some distress with dyspnœa, cyanosis, and a rapid pulse occurred in two primiparæ. One (Case 71) was the patient with heart block and embolic hemiplegia, who was delivered of a macerated hydrocephalic fœtus at the thirty-fourth week and died a few hours later. The other (Case 83) was admitted to the hospital as an urgency in the thirty-second week, on account of congestive heart failure. She went into labour the day after admission and died six weeks later from acute pulmonary œdema. One patient (Case 53) who had had two attacks of rheumatic fever and had complained of both dyspnœa and œdema prior to pregnancy, was delivered at the thirty-seventh week. The remaining four cases were only two weeks premature and presented no abnormal features.

Seventeen multiparæ were delivered prematurely by natural forces without distress and 14 had living children. Two of the multiparæ had albuminuria and symptoms of toxæmia prior to delivery, and labour occurred at the thirty-second and thirty-fourth week respectively ; in both cases the children were dead. In eight of the cases delivery occurred in the last two weeks of pregnancy.

Induction of labour.—Labour was induced in 12 cases, nine were primiparæ and three multiparæ. The reasons for induction in the case of the primiparæ were contraction of the pelvis in four cases, post-maturity in one, and the cardiac condition in the remaining four, and in the multiparæ the cardiac condition in one, and post-maturity in two.

In many cases during the later months of pregnancy the question arises as to whether a cardiac patient should be allowed to continue till full term, or whether the pregnancy should be interrupted as soon as the child is viable. If it is decided to terminate pregnancy, the next question is the method of doing so. In five of the patients in this series it was decided to interrupt the pregnancy on account of increasing cardiac distress. Two of these patients (Cases 38 and 60) had signs of congestive heart failure, and, although they responded to medical treatment, the condition of the heart was such that the further continuance of the pregnancy was considered inadvisable. Of the remaining three cases, two (Cases 21 and 65) had increasing dyspnœa and hæmoptysis, and the third (Case 35) showed slight recurrence of venous congestion in the neck at the thirty-eighth week, having had signs of impending heart failure at the seventh month.

(*d*) PROGNOSIS.—We are now in a position to compare the opinions which we formed on patients when they were first seen, with the final results. The cases in which we anticipated trouble may be divided into three groups : (1) Those which exhibited signs of congestive heart failure ; (2) those in which there was auricular fibrillation or heart block ; and (3) those which it was considered advisable to admit to hospital on account of increasing dyspnœa.

Of the six patients who had congestive heart failure, two died, three have been in poor health since confinement, and one only (Case 35) has done well. There were three patients with auricular fibrillation ; one of these has been included in the previous group on account of the presence of heart failure. She and one of the other two patients died, the third (Case 30), a second-para, aged 39, was delivered at full time and her condition does not seem to have deteriorated in any way as the result of her present confinement. The one patient with heart block also died.

Of the four patients who were admitted to hospital on account of increasing dyspnœa or hæmoptysis, one (Case 21) died from pulmonary embolism three days

after confinement. The other three (Cases 50, 63, and 65) have done quite well. In Case 65 in which, in addition to mitral stenosis there was aortic incompetence, labour was induced at the thirty-eighth week; the other two patients were normally delivered at full term.

These findings were summarized in Table VI. They showed that of the nine patients in the first two groups, four died, three have been in ill-health since confinement, while two only have got through without any apparent aggravation of their cardiac condition. Of the four patients in the third group whose symptoms were less severe, one died, and the other three have kept quite well.

Of the five fatal cases, four were primiparæ, while the fifth was a 14th-para who died two months after confinement and whose death was directly attributable to the fact that she neglected to observe the restrictions which her doctor had advised.

TABLE VI.—PROGNOSIS.

	Died	Ill	I.S.Q.	Total
1. Congestive heart failure	2	3	1	6
2. Auricular fibrillation and heart-block	2	—	1	3
3. Impending heart failure	1	—	3	4
Totals ...	5	3	5	13

(*e*) CONCLUSIONS.—As the result of these findings I think we may conclude that the outlook in pregnancy complicated by heart disease is not really so gloomy as some people imagine. In our series of 82 cases, five patients died, 12, in whom there were no complications up to the end of the puerperium, have since been lost sight of, and of the 65 who remain, 62 so far appear to have been none the worse. We expected trouble in the 13 cases with heart failure, persistent dyspnœa, and fibrillation. In eight cases our fears were realized, but in no other case in the series did we find evidence that the cardiac condition had been aggravated by the current pregnancy.

Valvular lesions gave us no help in prognosis. All the cases which went wrong could have been picked out without the use of the stethoscope, since all had either signs of congestive heart failure, auricular fibrillation, or heart block.

As regards cardiac enlargement, I am inclined to be less dogmatic than some previous writers [4]. Although, speaking generally, patients whose hearts are considerably enlarged do worse than those who have only a slight degree of enlargement, there are a considerable number of exceptions; six of the 12 patients in our series with the biggest hearts did quite well, while in three of our fatal cases the hearts were not very big.

Lastly, such extraneous circumstances as the financial position of the patient, and her ability and willingness to conform to the necessary restrictions of her activities, are all important in framing a prognosis.

With regard to treatment, I am of the opinion that pregnancy should be forbidden in all patients with established auricular fibrillation and in all those who are known to have suffered from congestive heart failure in the past. In the fibrillators, apart from the danger of heart failure, there is the risk of cerebral or pulmonary embolism.

When patients in this group are seen in the early months of pregnancy, the uterus should be emptied. When first seen at a later date, they should be kept at rest, and when the heart failure is relieved and the child is viable, Cæsarean section should be performed. I wish to emphasize the fact that the pregnancy should never be interfered with until the heart failure has been relieved by medical treatment.

One's opinion is often asked regarding the most suitable anæsthetic for the operation of Cæsarean section in patients with heart disease. Mackenzie [3] was of opinion that chloroform was unequalled in these cases, and stated that he had never seen any trouble when it was used. Personally, I am inclined to think that

chloroform in cardiac cases deserves more popularity than it at present enjoys. Spinal anæsthesia may be employed, but I hesitate to recommend it in cases where the systolic pressure is below 110.

In the less severe cases of heart disease, pregnancy may be allowed to proceed to full term, and a very great deal can be accomplished by careful supervision and medical treatment. In our series all cases in which the heart showed signs of giving way were admitted to hospital, and most of them responded promptly to treatment. I am convinced that many of these patients, had they not been treated in hospital, would in all probability have developed congestive heart failure.

Shortening of the second stage of labour by forceps extraction is undoubtedly of value in those border-line cases where there is considerable limitation of the cardiac reserve. Theoretically, the induction of premature labour should be of value in cardiac cases. Induction on account of the cardiac condition was performed in five cases in our series. The number is perhaps too small to justify us in drawing any general conclusions; but as the result of this experience, limited though it is, we would not advocate induction in these patients.

Let me summarize my observations by saying that, in the more severe types of heart disease, pregnancy should be forbidden, or terminated in the first three months; while in the less severe cases it should be allowed to pursue its normal course, under careful medical supervision.

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DISCUSSION ON FRONTAL SINUSITIS AND ITS TREATMENT.

Frontal Sinusitis: A Statistical Investigation.

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This paper contains an account of (1) all cases in which the frontal sinus was affected, treated by means of conservative methods and by intranasal operation, in the Ear and Throat Department of the Royal Infirmary, Edinburgh, during the years 1921 to 1930 inclusive, i.e., during the time which one of us (J. S. F.) has been in charge of the Department. (2) All cases seen in private practice from 1906 to 1930 inclusive. (3) All cases operated upon by one of us (J. S. F.) by the external route at the Royal Infirmary and in private practice (1907-1930).

We have not attempted to distinguish between catarrhal and suppurative affections of the frontal sinus.

The cases have, however, been divided into (*a*) acute and (*b*) chronic; the period of six months has been arbitrarily taken, i.e., all cases of over six months' duration have been regarded as chronic. The cases in which the frontal sinus was affected either alone or in conjunction with other paranasal sinuses, amounted to 338. Of these, 241 were acute and 97 were chronic.

A. Acute Cases.

These numbered 241 (94 right, 116 left and 31 bilateral). *Sex.*—160 were males and 81 females. The *Age* was ascertained in 207 cases, as follows: 11 to 20 years, thirty-five: 21 to 30 years, seventy-four: 31 to 40, fifty-eight: 41 to 50, twenty-nine: 51 to 60, seven: 61 to 70, four. *Duration.*—In 61 cases the trouble had only lasted one week; in 42, two weeks; in 19, three weeks; in 6, four weeks; in 1, five weeks; in 6, six weeks; in 2, seven weeks; and in 22, three months or over but less than six months. *Cause.*—Coryza or influenza was responsible for at least 142 and injury for 14 cases.

Symptoms.—In 230 cases the patients complained of frontal headache and in at least 183 there was marked periodicity of the pain. The usual time of onset was about 10 or 11 a.m., while the pain usually passed off at 2 or 3 p.m. In rare cases the pain began early in the morning (8 a.m.) and occasionally it did not come on

till the afternoon. In a few cases in which pus was under great tension, continuous pain of a throbbing character was present. It is noteworthy that in night nurses and others who are on night duty, the pain came on an hour or two after they got up, so that the period of onset probably depends upon the assumption of the erect posture. Tenderness on pressure over the anterior wall or floor of the frontal sinus was noted in 125 cases, while an orbital complication (swelling of the upper eyelid or abscess formation) was present in 23 patients.

Seasonal incidence.—January, 18: February, 31: March, 28: April, 30: May, 25: June, 16: July, 20: August, 12: September, 15: October, 19: November, 22: December, 15.

Examination.—Anterior rhinoscopy revealed pus in the anterior part of the middle meatus in 128, pus and polypus in 38, while in 57 cases pus was absent (total 223 cases). The septum was deviated to the affected side in 50 of the unilateral cases and to the non-affected side in 16 cases. Posterior rhinoscopy was carried out in 152 cases and showed that pus was present in 99, pus and polypus in 3, while in 50 cases no pus was found. Bacteriological examination showed that the most common organism was the streptococcus: next in frequency came pneumococci, staphylococci, influenza bacilli, diphtheroids and *B. coli*. Transillumination.—The frontal sinuses only were obscured in 95 cases, both frontals and antra in 93 (total 188). Radiography.—The frontal sinuses only were cloudy in 42 cases; the frontals, ethmoids and antra in 60: all sinuses obscured in 7 (total 109). It is noteworthy that in eight cases the frontal sinus appeared clear in the radiograms but was found diseased at operation.

Co-affection of other sinuses.—The maxillary antra and ethmoid cells were affected along with the frontal sinus in 135 cases, while in ten all the sinuses were affected on the side of the disease. (Note that in some cases, only transillumination was carried out and in others only radiography; in most cases, however, both methods of diagnosis were employed.)

Treatment.—Of the 241 cases (I) 161 were treated by conservative methods only, i.e., menthol inhalations, head light baths and analgesic powders. Irrigation of the frontal sinus has seldom been practised because it was found that in order to enter the frontal sinus with any certainty it was necessary to remove the anterior end of the middle turbinal and open up the anterior ethmoidal cells. If this were done it really amounted to intranasal operation on the frontal sinus, with provision of more or less free drainage. Thereafter the frontal sinus usually recovered without any irrigation. In acute cases in which the frontal, ethmoid and antrum were affected, intranasal operation on the antrum alone, with treatment by inhalations and possibly head light baths often effects a cure without any necessity for operation on the frontal sinus. Of the 161 cases, 105 were males and 56 females.

Results were ascertained in only 83 cases, as follows:—58 were cured by conservative methods; 17 were relieved (pain only coming on during acute coryza); in 6 pain and discharge are still present: in 2 operation was advised but refused. (Note that in previous "follow up" investigations we have found that only about 50% of patients can be traced.)

(II) *Intranasal operation: 66 cases.*—(Preliminary conservative treatment, as detailed above, was tried in 21 of the 66 cases.) As regards intranasal operation, local anæsthesia only was employed in 52 cases; in the remaining 14 both local and general anæsthesia were used. In all cases the anterior end and lower border of the middle turbinal was removed, the anterior ethmoidal and in some cases the posterior ethmoidal cells opened up with Grünwald and Blakesley forceps and the naso-frontal duct enlarged by upward-cutting forceps and the Watson-Williams rasp. Only in exceptional cases was any attempt made in the subsequent treatment to wash out the sinus with the cannula, dependence being as a rule placed upon the freer drainage obtained by the above method. In 12 cases submucous

resection of the septum was performed in addition to the above procedure. In 24 cases, in addition to intranasal operation on the ethmoid and frontal, the maxillary sinus was drained, while in five cases the sphenoidal sinus was also opened by the intranasal route.

Complications.—One patient developed erysipelas and another scarlet fever. In several cases there was extravasation of blood at the inner angle of the orbit.

Results.—A cure was obtained in 34 cases; in three the patient reported slight recurrence of frontal pain if suffering from coryza; in eight cases the nasal discharge continues, but the patients have no pain. In 21 cases the result is unknown.

(III) *External operation* was performed in 14 cases (2 right, 6 left and 6 bilateral). Five of the 13 patients had had previous operations performed, e.g., submucous resection of the septum, opening up of the ethmoidal cells, drainage of the maxillary antrum, intranasal operation on the frontal and sphenoidal sinuses. With regard to the external operation on the frontal sinus: Two recent cases were operated upon by removal of the floor of the sinus, together with opening up of the anterior ethmoidal cells and removal of most of the paper plate of the ethmoid, lachrymal bone and also of the frontal process of the superior maxilla and of the middle turbinal (modified Howarth operation). In these cases iodoform gauze was introduced into the frontal sinus, and the end brought down into the nasal cavity, the external wound being closed by silkworm-gut sutures. The packing and stitches were removed in two or three days. One of these patients died (Case VIII). One case was operated upon by the Killian method. In eleven cases complete obliteration of the frontal sinus was carried out, the anterior wall and floor of the sinus and also the supra-orbital ridge being removed and the mucosa curetted from the posterior wall. In addition, the middle turbinal and ethmoidal cells were more or less completely removed, and in many cases the sphenoidal sinus was also opened through the external incision. At the end of the operation gauze packing was introduced into the cavity between the superficial tissues and the posterior wall of the sinus. One end of the gauze packing was brought out at the external end of the incision, which was otherwise closed with silkworm-gut sutures. The other end of the packing was brought into the nose and was removed in two days. A certain amount of œdema of the upper eyelid occurred in many cases, but soon disappeared. It must be admitted that in many of these cases there is a considerable amount of deformity, depending on the size and depth of the sinus. On the other hand, in the opinion of the writers, the safety of the operation over that obtained by Killian's method more than compensates for the danger of deformity.

Conditions found.—Pus and "granulations" in 12, pus and polypoid mucosa in two.

Complications.—Two patients had slight fever after operation, several had temporary diplopia; one patient developed pneumonia, but recovered. One patient had frontal lobe abscess, and recovered (Case III). Two patients had meningitis on admission and died. One had cavernous sinus thrombosis on admission, and died. The remaining patient had septicæmia on admission and died.

Results.—In five a cure was obtained; one reports improvement, but not cure; in four no report was obtained; as stated above, four patients died.

B. Chronic Cases.

Patients in whom the frontal sinusitis had existed for more than six months numbered 97 (30 right, 40 left and 27 bilateral): 51 patients were male and 46 female. *Age.*—1 to ten years, one; 11 to 20, nineteen; 21 to 30, nineteen; 31 to 40, six; 41 to 50, six; 51 to 60, eight; 61 to 70, two; 71 to 80, two. *Cause.*—This was

more difficult to ascertain than in the acute cases, but in at least 24 the frontal sinus trouble was attributed to coryza or influenza, two cases were due to scarlatina and three to injury. The seasonal incidence does not appear to be of much importance in the chronic cases.

Symptoms.—Frontal headache was complained of in 64 cases, but marked periodicity of the headache was noted in only 22.

Examination.—Tenderness over the frontal sinus was present in 36 and an orbital complication in 23. *Anterior rhinoscopy* showed pus in the middle meatus in 36, pus and polypus in a further 41 cases; pus was absent in 16. The septum was deviated to the affected side in 13 cases and to the non-affected side in 7. On *posterior rhinoscopy* pus was noted in the middle meatus in 26 and pus and polypi in 21. In a further 24 cases no pus was noted. *Transillumination.*—In 17 cases the frontal sinus only was obscured, in 58 the frontal sinuses and antra were dark. *Radiography.*—Frontal sinuses only, cloudy in 10; frontals, antra and ethmoids in 36: all sinuses cloudy in 16. It is worthy of note that in four cases the frontal sinuses appeared clear in the radiograms but at operation were found to be diseased.

Co-affection of other sinuses.—The ethmoids and maxillary antra were affected in 55 cases, while pansinusitis was present in 13 (total 68 cases out of 97).

Treatment.—(I) In 18 cases the patients would only consent to conservative treatment, though two of these patients had submitted to submucous resection of the septum and seven to drainage of the maxillary sinus.

Results.—Nine of the patients were relieved: eight remained in statu quo: in one no report was obtained.

(II) *Intranasal operation: 39 cases.*—Local anæsthesia only was employed in 20 cases, while in the remaining 19 both local and general anæsthesia were used. In all of the cases the frontal sinus was drained by the intranasal route according to the method described under (A). Submucous resection of the septum was performed in three cases and drainage of the maxillary antrum in 17, in addition to the frontal sinus operation. In three cases the sphenoidal sinuses were operated on by the intranasal route.

Results.—Cure, 18; no pain but discharge continues, 6; still pain and discharge, 6. One death from septicæmia. No report, 8 cases.

(III) *External operation* was performed in 40 cases (11 right, 14 left, and 15 bilateral). Of the 40 cases 31 had already been operated upon as follows. Removal of polypi, 6; drainage of antra, 10; operation on antrum, ethmoid and sphenoid, 2; submucous resection of septum in addition to operation on antra and ethmoids, 3; submucous resection of septum with removal of nasal polypi, 2; submucous resection and operation on sphenoid, 1; intranasal operation on frontal and maxillary sinus, 1; previous external operations on frontal sinus elsewhere, 6 cases. With regard to the operation on the frontal sinus performed by one of us (J. S. F.) we find that the modified Howarth operation was carried out in nine cases, the Killian operation in two cases and the radical operation (complete obliteration) in 29 cases (in two of these 29 cases the Killian operation was performed first of all but had to be converted into the radical operation owing to necrosis of the bridge).

Contents of the sinus.—Pus and "granulations," 27 cases: pus and polypoid tissue, 10 cases: mucocele, 3 cases (note that in these three cases the modified Howarth operation was performed).

Complications.—Severe fever, 1: slight fever, 3: pneumonia with recovery, 1: cavity re-opened on account of persistent œdema, 1; serous meningitis with recovery, 2; septicæmia with recovery, 1; corneal ulcer with complete recovery of vision, 1; meningitis and death in 3 cases.

Results.—A cure was obtained in 21 cases: improvement, but not a cure in 2: no report, 14 cases; death, 3 cases.

ILLUSTRATIVE CASES.

(I) *Bilateral Chronic Frontal and Ethmoidal Sinusitis.*—J. R., male, aged 33, seen 2.4.24. Bilateral frontal headache for five years with marked periodicity: previous external operations in Rhodesia. Discharging fistula above right eye; pus and polypi in both middle meatus; frontals, ethmoids and sphenoids blurred in radiograms. Complete bilateral operation, 3.4.24; fistula present; pus in sinuses which extended to external angle on both sides; iodoform gauze drainage for two days; œdema of eyelids. Recurrent suppuration, 7.10.26; ethmoidal extension cleared out: cure.

(II) *Chronic Pansinusitis.*—S. S., male, aged 38, seen 20.3.25. Bilateral frontal headache for ten days, with periodicity; right middle turbinal polypoid and pus present. Conservative treatment tried. S.M.R., followed by intranasal operation on frontal sinuses in 1927. Complete frontal sinus operation on both sides 6.9.29; pus present (*Pneumococcus* and *B. mucosus capsulatus*); iodoform gauze packing removed in three days; temporary diplopia after operation; patient cured.

(III) *Acute Left Frontal Sinusitis; Abscess of Left Frontal Lobe; Operation; Recovery.*[1]—G. L., male, aged 29. Influenza 10.2.22; slight ptosis (left); slight fever; continuous headache and throbbing pain behind left eye. 22.2.22.—Jacksonian fit affecting right face, arm and leg, lasting one and a half hours, preceded and succeeded by loss of speech for a short time.

2.3.22.—First examination by J. S. F. showed no swelling of mucosa or pus in the nose; tenderness present over left frontal sinus; transillumination showed all sinuses dark and radiograms demonstrated blurring of all sinuses. 3.3.22.—Frequent vomiting; pulse 38; early optic neuritis; slow speech; absence of abdominal reflex and presence of Babinski's sign on contralateral (right) side; brain abscess diagnosed by Professor Bramwell. *Operation.*—General anæsthesia; pus under pressure in left frontal sinus; posterior wall removed; granulations on outer surface of dura; large quantity of odourless pus evacuated from left frontal lobe (pneumococcus); recovery.

A year or two later the patient developed status epilepticus. The left frontal lobe was again investigated but no recurrence of abscess was found; large trephine opening made over Rolandic area on left side by Professor Wilkie and Mr. Norman Dott but nothing abnormal found. The patient recovered. 29.3.31.—Patient very well.

(IV) *Osteoma in Left Frontal Sinus.*—M. S., female, aged 37, seen 26.5.30 complaining of pain over the left side of the nose. On anterior and posterior rhinoscopy both sides of the nose appeared normal. Radiograms showed a dense shadow in the left frontal sinus.

14.6.30.—General anæsthesia; radical frontal sinus operation. Killian incision with vertical cut on forehead; thin anterior wall of sinus removed and osteoma exposed; the outline of the bony growth followed the contours of the sinus and resembled the Prince of Wales' feathers. The growth was rooted in the lower part of the sinus. The floor of the sinus was also removed. There was a little mucus or thin mucopus between the osteoma and the narrow remaining cavity in the upper part of the sinus. A large opening was made into the nose, most of the middle turbinal being removed and the anterior ethmoidal cells freely opened. The cavity was packed with iodoform gauze and the external wound sutured except at the outer end, which was drained; satisfactory progress. 12.11.30.—Deformity slight; nasal cavities look well.

(V) *Acute Bilateral Frontal Sinusitis with Pachymeningitis Externa and Interna; Death.*—A. M., female, aged 21, seen 16.8.09. Coryza six weeks ago; frontal headache two weeks, with swelling above left eye; shivering attack five days ago, with stoppage of nasal discharge. On admission: drowsy; marked tenderness in left frontal region; temperature 103° F.; pulse 104; respiration 32. Pus in left middle meatus. Immediate operation: pus in both frontal sinuses. Lumbar puncture gave fluid under great pressure. 17.8.09.—Temperature 105° F. 18.8.09.—Patient very drowsy; internal strabismus left eye. Second operation—posterior wall of left sinus removed; foul greenish pus evacuated (numerous organisms); dura opened; brain explored, but no abscess; hernia cerebri formed. 19.8.09.—Death. *Post-mortem.*—Extensive meningitis between dura and arachnoid, over cortex and, to a less extent, in middle fossa.

(VI) *Acute Pansinusitis (left); Cavernous Sinus Thrombosis: Operation; Death.*—J. O. B., male, aged 45, suffered from nasal catarrh and sore throat 16.12.19. Discharge

[1] See *Journ. Laryng, Rhin. and Otol.*, 1922, xxxvii, 525.

stopped and a painful swelling appeared at upper and inner angle of left orbit 18.12.19. Temperature 101° F. Patient first seen and admitted 20.12.19 with proptosis and restricted movements of left eyeball and chemosis of conjunctiva (cavernous sinus thrombosis). Nasal septum almost blocked left nostril; tongue dry.

Immediate operation.—Local anæsthesia; intranasal operation on left ethmoid; no pus.

Evening temperature 102° F.; patient delirious. 21.12.19.—Second operation: general anæsthesia; Killian incision; left frontal, ethmoidal and sphenoidal sinuses opened; mucosa congested; no pus; wound left open. For the next three days evening temperature rose to 103° F.; pulse and respirations accelerated. 26.12.19.—Patient much better; swelling of eyelids decreased and movements of left eyeball improved. Dr. J. V. Paterson reported congestion of veins of fundus, but no optic neuritis. 27.12.19.—Congestion of base of right lung; respirations rapid.

29.12.19.—Delirium alternating with coma; third operation; general anæsthesia; posterior wall of left frontal sinus removed; no extradural abscess; no subdural abscess or abscess of frontal lobe. 1.1.20.—Kernig's sign present; deep coma; temperature 103° F.; death.

Post-mortem.—Purulent meningitis over both frontal lobes; slight meningitis at base; gelatinous mucopus in left maxillary antrum (staphylococcus, pneumococcus and diphtheroid bacillus isolated).

Microscopic examination by Dr. Logan Turner and Dr. Reynolds (*Journal of Laryngology and Otology*, 1927, vol. xlii, p. 181) showed infiltration of mucosa of sphenoidal sinuses by pus cells, with hæmorrhages; almost complete obliteration of the blood spaces of the left cavernous sinus by fibrous tissue; some pus and blood-clot were also present in the cavernous sinus. Dr. Turner and Dr. Reynolds regarded the sphenoidal sinuses as the focus of infection.

(VII) *Acute Suppuration in Frontal, Ethmoidal and Sphenoidal Sinuses; Purulent Lepto-meningitis; Death.*—A. S., male, aged 19, admitted 22.3.29. Influenza three weeks before admission; constant supra-orbital headache for one week, with swelling of lower part of forehead. On admission occipital headache present; patient drowsy; temperature 103° F.; pulse 112; tongue furred and breath foul; fluctuating swelling over glabella; eyelids on both sides œdematous. Pus on anterior and posterior rhinoscopy. *Immediate operation.*—General anæsthetic; double Killian incision; erosion of anterior wall of right frontal sinus; foul pus present in both sinuses (non-hæmolytic streptococcus); inter-sinus septum perforated; anterior wall of both sinuses removed; mucosa necrotic; posterior wall of sinuses very pale. Ethmoidal cells cleared out and sphenoidal sinuses freely opened; all contained pus.

24.3.29.—Patient very restless; temperature elevated; coma, followed by death.

Post-mortem.—Purulent meningitis present over right hemisphere from vertex to base (pneumococcus and Pfeiffer's bacillus); no abscess present.

Remark.—There can be no doubt in this case that purulent meningitis was present on admission.

(VIII) *Acute Frontal, Ethmoidal and Sphenoidal Suppuration (left); Septicæmia: Meningitis; Death.*—S. B., male, aged 28, first seen 25.4.30. Recent left frontal headache and nasal discharge. Examination showed œdema of conjunctiva and proptosis, with limitation of movements of left eye and reduced vision. Pus present in both nasal cavities; tenderness over left frontal sinus; left frontal and maxillary sinuses dark on illumination. Radiograms showed little difference between right and left side (radiograms often unreliable); temperature 102° F. 26.4.30.—Left middle turbinal removed and ethmoid opened up; left sphenoid opened; modified Howarth operation left frontal sinus; pus obtained (*Staphylococcus aureus*). 28.4.30.—Less bulging of eyeball; still œdema of conjunctiva but eye movements better; no optic neuritis; temperature 102° F.; abscess in gluteal and deltoid regions opened (*S. aureus*). 29.4.30.—Blood-culture shows *S. aureus*. 2.5.30.—Evening fever continues; general condition unsatisfactory; hypertonic saline given intravenously. 14.5.30.—Evening fever continues; tenderness over both frontal sinuses and left antrum. Second blood-culture shows hæmolytic streptococcus. 19.5.30.—Deltoid and gluteal abscess healed; edges of Killian incision have come apart. 22.5.30.—Edges of wound pared and stitched. 28.5.30.—Blood-culture negative. Signs of old tuberculous lesions at both apices, with definite cavities. 4.6.30—Patient mentally peculiar, refuses to speak. 6.6.30.—Kernig positive; cerebrospinal fluid turbid and under pressure (*Pneumococcus mucosus* present on culture); slight dysphagia present; death. *Post-mortem.*—Extradural abscess in left frontal

region; inner table eroded; cario-necrosis of posterior wall of frontal sinus and of roof of sphenoid; small sequestra present; mucus only present in left frontal, ethmoidal and sphenoidal sinuses; mucopus also present in right frontal sinus; no thrombosis of venous sinuses but early leptomeningitis present over both hemispheres (*S. aureus* and *P. mucosus* obtained on culture).

(IX) *Chronic Pansinusitis; Septicæmia: Empyema; Death.*—D. M., male, aged 36, seen 24.2.20. Frontal headache with nasal obstruction and discharge for several years; previous removal of nasal polypi. Deviation of septum; pus in left middle meatus and roof of nasopharynx. Radiograms showed all sinuses cloudy. 26.4.20.—Local anæsthesia; S. M. R.; intranasal operation on right frontal and both ethmoids and sphenoids. 28.4.20.—Evening temperature 99·6° F.; pain in joints and limbs. 30.4.20.—Profuse perspiration; temperature 104° F. 2.5.20.—Dullness at right base; pus withdrawn. 3.5.20.—Rib resection and drainage of empyema (pure culture of streptococci); patient delirious. 4.5.20.—Death. *Post-mortem.*—Old tuberculous foci in left lung, with adhesions; right lung collapsed; brain membranes congested; brain œdematous; no evidence of bone disease, meningitis or venous thrombosis.

(X) *Chronic Suppuration in Left Frontal Sinus; Radical Operation; Purulent Lepto-meningitis: Death.*—D. McI., male, aged 23. History of shrapnel wound involving left eye and cheek in 1916: submucous resection and Caldwell-Luc operation on left maxillary antrum, with removal of piece of shrapnel in 1919. Patient admitted 8.2.21: pus in left middle meatus; sinus discharging pus below left eyebrow; radiogram showed left frontal and ethmoidal cells obscured.

21.2.21.—External operation on left frontal sinus: cavity contained thickened mucosa and pus. While curetting a cell on the posterior wall of the cavity, a slight escape of cerebrospinal fluid occurred. Careful disinfection and free drainage of the cavity carried out.

24.2.21.—Patient restless and vomiting: temperature 102° F.: severe headache present. Lumbar puncture evacuated turbid cerebrospinal fluid (pneumococcus present). Wound opened up and posterior bony wall of sinus removed: dura mater covered with granulations and adherent to bone: dura opened but no pus evacuated: hypertonic saline gauze packing. 25.2.21.—Death.

Post-mortem.—Recent purulent meningitis over left frontal lobe: an area of old meningitis present in region of left olfactory bulb: no brain abscess.

(XI) *Chronic Suppuration in Right Frontal and both Maxillary Sinuses; Meningitis; Death.*—W. S., male, aged 42, admitted 21.6.22. History of small abscess above right inner canthus opened by his doctor eighteen months before admission. Anterior and posterior rhinoscopy showed no pus: transillumination and radiograms showed dullness of frontal, ethmoidal and maxillary sinuses. Proof puncture evacuated foul pus from both antra.

6.7.22.—Radical operation right frontal sinus: fistula in floor of sinus; mucosa congested and thickened; pus in cavity; most of lachrymal bone and lateral mass of ethmoid removed; iodoform gauze packing; partial drainage of external wound. 13.7.22.—Wound healed. 19.7.22.—Carious teeth extracted.

1.8.22.—General anæsthesia; radical operation on both maxillary antra; mucosa swollen and foul pus present. 8.8.22.—Slight evening fever. 15.8.22.—Remains of right middle turbinal removed. 18.8.22.—Evening temperature 103·2° F.; occipital headache; slight neck stiffness; Kernig positive. Lumbar puncture: fluid turbid and under pressure (long-chained diplo-streptococci). 21.8.22.—Fever continues but there is less retraction of head; patient sleeps well. 22.8.22.—Temperature 100·2° F.; pulse 68; no vomiting; no optic neuritis. Neurologist suspects frontal lobe abscess. *Third operation.*—Killian incision re-opened: frontal sinus quite obliterated; posterior wall removed with gouge; dura normal; dura opened and frontal lobe explored with negative result; left frontal sinus investigated but found healthy.

24.8.22.—Death. *Post-mortem* examination showed small hole in roof of nose on right side at the point where the cribriform plate joins the small wing of the sphenoid: sphenoidal sinus healthy. Meningitis, however, was more marked on left side though there was no apparent lesion in the roof of the nose on this side.

(XII) *Chronic Suppuration from Sinus above Inner Canthus (left side); Radical Operation; Meningitis; Death.*—Mrs. J. R., aged 80, seen 1.2.24 suffering from purulent nasal discharge of many years' duration and from discharge of foul pus from a sinus above the inner canthus on the left side. Anterior and posterior rhinoscopy showed polypi and pus in the middle meatus. On transillumination both frontal sinuses and left antrum dark. Radiograms showed extensive left frontal sinus.

5.2.24.—General anæsthesia: radical operation left frontal sinus; Killian incision; large hole in floor of left frontal sinus, surrounded by very soft bone; foul pus in sinus; posterior wall eroded in several places; left middle turbinal removed and ethmoidal cells cleared out; iodoform gauze packing with intranasal drainage.

Progress fairly satisfactory till 9.2.24, when there was sudden loss of consciousness at 10.30 p.m. Temperature 100·6° F.

11.2.24.—Death. *Post-mortem.*—Purulent meningitis; ventricles slightly dilated; red softening in anterior part of left frontal lobe; lungs showed pleurisy and hypostatic congestion; mitral and aortic valves diseased and aorta atheromatous.

Mortality.—There were 105 intra-nasal operations with one death and 54 external operations with seven deaths.

Dr. J. P. Stewart said: Dr. Fraser and I wish to apologize for the dullness of our paper. Our excuse is that it involved at least six months' hard work; and secondly, that it does give an accurate account of the subject as far as lies in our power.

With regard to the cause of the periodicity of pain in frontal sinusitis, our own view is that it is due to the assumption of the erect posture and, in support of this, we may mention a case in which the pain came on at the usual time—10 a.m.—but passed off when the patient lay down.

There is a considerable difference between the symptoms met with in acute and chronic cases. For instance, frontal headache was present in at least 95% of the acute as compared with only 66% of the chronic; periodicity of the pain was noted in 76% of the acute and in only 23% of the chronic, while tenderness on pressure was found in 52% of the acute and in only 37% of the chronic cases.

As regards co-affection of the other sinuses, we may note that this was more frequent in the chronic (70%) than in the acute cases (60%).

It is of interest that nearly fifty of our cases were referred to the Ear and Throat Department from the Ophthalmological Department to which the patients had first of all been sent by their own doctors. It is evident that many general practitioners are, as yet, ignorant of the symptoms and signs of frontal sinus suppuration. They appear to think that supraorbital headache, with pain and tenderness over the eyebrow region, is due to some visual disturbance.

It has been found that neither transillumination nor radiography is absolutely to be relied on in the diagnosis of frontal sinusitis. In some cases the affected sinus transilluminated, but was cloudy in the radiogram. In others the affected sinus did not illuminate, but appeared clear in the radiogram; we refer of course to cases in which operation showed pus to be present. We recommend, therefore, that these two methods of investigation should be carried out consecutively and the results compared. It would then be possible to form a fairly accurate idea of the condition of the suspected sinuses.

In acute cases of middle-ear suppuration it is very common to have an acute maxillary sinusitis on the same side, but rare to have the frontal sinus also affected.

It is noteworthy that patients are far more willing to allow radical operations on the maxillary antrum than on the frontal sinus; no doubt this is because the latter involves a scar on the face. In this connection we admit that in many of our radical frontal sinus operations there is considerable disfigurement. Many of these cases were operated on after it had been found that Killian's operation was unsatisfactory, and even dangerous, but before the publication of Mr. Howarth's paper. We intend in future to make more frequent use of Mr. Howarth's procedure, especially in acute cases.

We believe that incision in the (unshaven) eyebrow line leaves a less noticeable scar than when the incision is made beneath the eyebrow. This is especially marked in our recent acute cases, in which the Howarth operation was performed.

The rapidity of healing after the Killian incision is remarkable; this no doubt is due to the excellent blood supply of the part.

Though the removal of part of the frontal process of the superior maxilla and of the paper plate of the ethmoid involves the exposure of the tear sac and the groove in which it lies, it is noteworthy that tear sac troubles very seldom follow external operation on the frontal sinus and ethmoid. In our series there is only one case in which epiphora followed operation.

The Treatment of Frontal Sinusitis by Intubation: An Analysis of Sixty-three Cases.

By Douglas Harmer, F.R.C.S., and Bedford Russell, F.R.C.S.

During the last ten years we have operated on sixty-three cases with steadily improving results. A few of them were treated by Mr. Rose, Mr. Just, and clinical assistants. Now the operation is employed by other surgeons both in this country and also in South Africa, America and elsewhere,[1] and enthusiastic reports have been received about it.

The operation.[2]—The affected side of the nose is sponged and packed with gauze soaked in a solution of cocaine and adrenalin fifteen minutes before the operation. The forehead and eyebrow are painted with tincture of iodine but not shaved. The size and position of the sinus are determined by examination of a radiogram. Under general anæsthesia an incision, three-quarters of an inch long, is made immediately below the inner end of the eyebrow. On no account should it extend outwards far enough to expose or divide the supra-orbital nerve. In some of our earlier cases the incisions were too long and the nerves afterwards became involved in the scars, resulting in persistent neuralgia or discomfort.

All the tissues are then divided, including the periosteum just above the supra-orbital margin. Bleeding vessels are ligatured with fine catgut, the periosteum is reflected upwards and a mastoid retractor is introduced, thus exposing a small area of bone. With a gouge and mallet an opening is made into the sinus above the supra-orbital ridge, large enough to admit the tip of the little finger. The centre of the opening should be three-eighths of an inch from the middle line, a point usually directly above the infundibulum.

The mucosa is thus exposed and may be thin, pale and retracted when the infundibulum is occluded (vacuum cases) or greatly congested, plum-coloured and pouting when the sinus is distended with pus. Before opening it the whole wound should be smeared with bipp. The mucosa is then divided and secretion is removed by suction. A thin silver probe bent in a circular form—or even better, as suggested by Mr. Pavey Smith, a flexible gold wire from a spectacle frame—is passed through the infundibulum into the nose, its lower end being seized and dragged outside the anterior naris. In some cases difficulty may be experienced in finding a passage into the nose, owing to constriction of the lower end of the infundibulum, and much time can be saved at this stage by removing the anterior end of the middle turbinate, if present, and opening the anterior ethmoidal cell. When this is done,

1 See *Journ. Laryng., Rhin. and Otol.*, 1922, xxxvii, 525.

2 First described in "Modern Operative Surgery" by H. W. Carson, 1924, ii, 265.

the probe passes easily in most cases. Rarely, the bony canal may be so constricted and tortuous that the probe cannot be passed without force, which should be avoided as far as possible, as the success of the operation largely depends on avoidance of trauma. If the probe is not sufficiently curved, the lower end may pass down to the floor of the nasal cavity and, if blood is present, may be difficult to find.

A long piece of stout linen thread is tied to its lower end and the probe is withdrawn so that the thread is pulled through the infundibulum and out of the wound above the eye. A soft rubber catheter is attached to the lower end of the thread and pulled through into the wound. It is essential that it should be small enough to pass through the duct without damaging or stripping its lining. In rare instances this may be impossible, in which case the thread only should be retained without a tube. A day or two later, when the congestion has subsided, the tube can easily be introduced.

The upper end of the catheter is cut off and a small piece is attached to it transversely so as to anchor it to the forehead and prevent it slipping out into the nose. The external wound should again be bipped but not closed by sutures (except in vacuum cases without discharge), as it is better to have free drainage above and below in the early stages of the treatment. A very light dressing is applied to the wound and should be changed frequently, if necessary being replaced by fomentations.

The operation can usually be completed within fifteen minutes and causes so little shock that the patient can leave his bed within a day or two.

After-treatment.—For about a week a cannula should be passed into the catheter and employed to irrigate the wound daily with normal saline or peroxide of hydrogen. After this the discharge usually ceases in acute cases and the wound closes down around the tube, but it is generally advisable to intubate for longer periods. In cases of chronic sinusitis it is necessary for the patient to wear the tube for several months. This causes no discomfort and does not prevent his returning to work after a few days. After about ten days the tube is generally so loose that it can be replaced by one of a larger size, and this replacement should be repeated at regular intervals, the principle of the treatment being the gradual dilatation of the fronto-nasal duct by elastic pressure, which is so slow that its lining is not damaged. If the tube is not enlarged too rapidly, the patient experiences no discomfort. Conversely, if too large a tube is introduced, either at the operation or later, it may cause great pain or even œdema of the eyelid.

During the first week or so of the treatment we have found it advisable to pull the tube through the wound so that there is free drainage externally, as well as into the nose; otherwise the tissues around the wound may become inflamed, swollen and painful, recovery being much delayed. Later this is not necessary. If a tube has to be worn for many weeks it need only be drawn up so that its upper end is lying in the sinus, in which case it is anchored to the forehead by strings passed through and tied to a small rubber button.

Changing the tube.—If the tube is anchored outside the forehead, a thread should be attached to its lower end and the catheter slowly withdrawn through the external wound. By this means the thread is drawn through the duct and, after the nose has been sprayed with cocaine, can be used to pull up a larger catheter into the sinus. If there is much discharge, it is advisable, before introducing the new tube, to pass an ordinary antrum cannula either from below or above and wash out the sinus thoroughly.

If the tube is attached to a button and does not project through the wound on the forehead, a thread should be fixed to the string behind the button which is then detached and the tube is drawn downwards out of the nose.

In most of the cases no regular irrigation has been carried out, but quicker recovery is obtained if the patients wash through the catheter daily and, better still, if

they can attend regularly for this treatment. In many of the cases the size of the tubes has never been increased because the patients were hospital out-patients and did not attend regularly. This accounts for a number of failures. As a rule, it is necessary to begin with about a No. 3 catheter and in a chronic case to enlarge gradually up to a No. 7 or 10, by which time the duct should be permanently dilated and the tube can be removed.

Given these conditions, it has been found that a large antrum cannula can often be passed easily into the sinus without cocaine, and, if necessary, the patient can be taught to pass the cannula himself and wash out the sinus regularly.

By this simple operation it is possible to dilate the fronto-nasal duct permanently. Bone absorption takes place around the tube. A straight canal is produced lined with unscarred epithelium and does not tend to contract after removal of the tube. With careful after-treatment the majority of cases can be relieved—many of them cured—without disfigurement, or with certainly far less than is caused by many other forms of radical operation.

Summary.—During the last ten years, sixty-three cases of frontal sinusitis have been treated by intubation. The operation has proved simple to carry out and absolutely free from danger. Because of its simplicity it has been possible to perform it on many patients to whom one would have hesitated to recommend more serious radical treatments.

The aim of the operation is twofold. First to provide free drainage and ventilation, both externally and internally. Secondly to dilate the bony fronto-nasal canal without damaging its lining membrane. Intubation with an elastic tube fulfils both these requirements, and if the tube is slowly enlarged it does not cause any irritation or inflammation. On the contrary, the lining of the sinus in most cases rapidly recovers. In successful cases, a straight passage from the nose to the sinus is obtained, through which a cannula can be passed easily. If necessary, a patient can be taught to pass a cannula and wash out the sinus regularly. In some cases, after a period of years, it may be difficult to find the entrance to the infundibulum, especially if there is an obstruction in the nose, such as a deflected septum or enlarged ethmoidal cell. But failure to pass the cannula seldom results in a return of the symptoms. The cases in which the treatment is likely to fail are those in which there has been long-standing inflammation which has caused scarring of the soft tissues and particularly those in which there have been numerous previous operations. In many of the latter the ducts no longer exist, having been replaced by masses of scar tissue. Another cause of failure has been involvement of other sinuses, notably when the opposite frontal sinus is infected and communicates with the one that has been intubated. In such cases re-intubation may be necessary. In 15 cases in which the patients were suffering from acute sinusitis, pain has been permanently relieved in 12 and discharge in 10. One patient died from cerebral abscess. In 35 cases of chronic sinusitis, pain was relieved in 16 and discharge in 19. Two patients died: one from erysipelas, two years later; the other committed suicide.

In five cases of vacuum sinusitis and eight cases of mucoceles all obtained relief. External fistulæ can always be cured.

In a large percentage of cases the wounds healed up so well that the scars were almost invisible. The absence of deformity as compared with that in many other external operations is remarkable. With this treatment, the patient is only confined to the house for a few days. He generally obtains immediate relief from pain. His nerve symptoms rapidly disappear and the general health soon recovers. The patients have experienced no discomfort from the tubes; on the contrary, in those cases in which symptoms have recurred they have frequently asked for the tubes to be replaced. There has been no fatal result directly attributable to the operation. The method has proved so satisfactory that it has become the routine treatment at

St. Bartholomew's Hospital for all forms of frontal sinusitis that cannot be cured by intranasal treatments.

[Eleven cases were shown illustrating the method of treatment described in the paper. Four of the patients had suffered from acute sinusitis, six from chronic sinusitis, and one had had a mucocele.]

The Treatment of Chronic Frontal Sinusitis.

By WALTER HOWARTH, F.R.C.S.

THERE is no doubt that the majority of acute sinus inflammations tend to undergo spontaneous healing and that this occurs not only in the catarrhal variety, but in the purulent ones as well. The main factor in this resolution of inflammation is the possibility for the products of inflammation to escape freely from the affected sinus, and anything that militates against this free escape must inevitably retard the healing process.

In the frontal sinus there are many factors which may interfere with free drainage and aeration, and the presence of any one of them may be sufficient to cause the inflammatory condition to pass over from the acute to the chronic stage. Naturally, mechanical factors, such as high deviations of the septum (fig. 1) and displacements of the middle turbinate or overgrowths of it (figs. 2 and 3) (perhaps owing to an accessory cell within it) may obstruct the fronto-nasal duct, and we are all familiar with cases in which a bilateral frontal sinusitis has failed to undergo resolution on one side, owing to the presence of some such hindrance to drainage. Anatomical variations in the fronto-nasal duct itself, particularly in the disposition of the anterior ethmoidal cells around it (fig. 4), are potent factors in the delay of the healing process, and the development in this region of inflammatory processes, such as polypi or local hypertrophic conditions, so often seen in those whose occupation is a dusty one, will also favour the chronicity of the inflammation. To what extent the degree of virulence and nature of the infecting organism play a part I have never been able satisfactorily to determine, but an exceptionally viscid type of secretion or intense congestion in the mucosa near the outlet of the sinus will favour stagnation and so delay resolution. It is certainly true that infections due to the influenza bacillus more frequently lead to chronic sinusitis than infections due to other organisms.

Free drainage is not the only essential for resolution to occur, and we must never forget that aeration and proper ventilation of the affected regions are also necessary. Nor should we forget that resolution, though complete enough to provide for cessation of symptoms, may not, in fact, be really complete, and that frequent acute attacks resulting in a progressively imperfect resolution may indeed result in a chronic suppuration.

This brief outline of the pathogenesis of the condition is not, I think, beside the mark, since it is essential that the treatment should be based upon the pathology of the condition. This is no place in which to discuss the endless variety of treatment that may be adopted to meet the varying conditions, and it will, I hope, best fulfil the objects that we have before us if I mention the various procedures that I am accustomed to adopt and indicate in some way how these are carried out.

It has always been my endeavour to adopt the simplest measures that may be necessary in each case and to interfere as little as possible with the natural process of repair. As a rule, cases in which the infection has lasted for a comparatively short time will require a relatively simpler procedure than those in which the disease is of considerable duration. When nasal obstruction is a marked feature on the

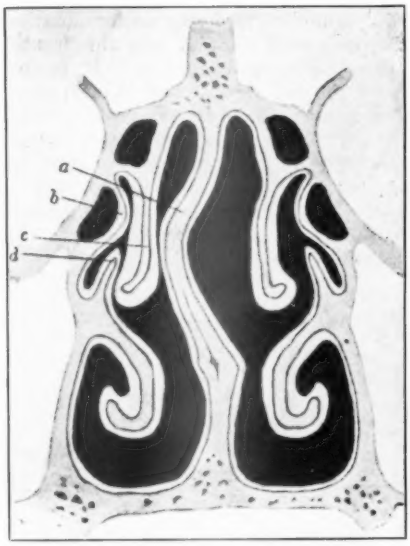

FIG. 1.—High deflection of the septum.

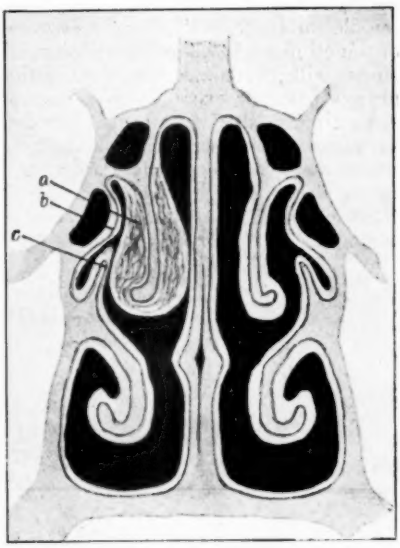

FIG. 2.—Overgrowth of the middle turbinate.

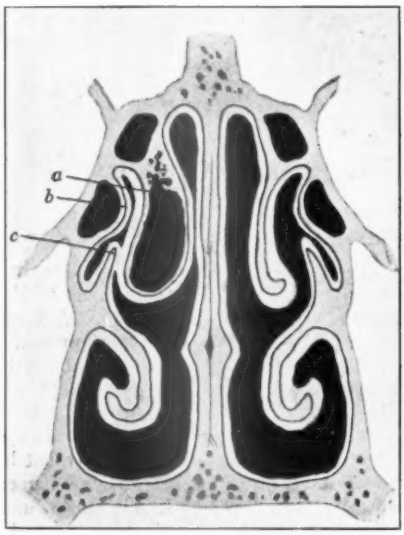

FIG. 3.—Accessory cell in middle turbinate.

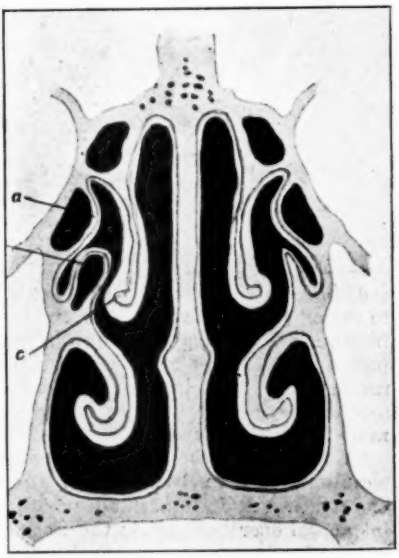

FIG. 4.—Cell in uncinate process.

affected side, relief of this, together with the removal of the anterior end of the middle turbinate, will relieve pressure on the infundibulum and provide for aeration of the ethmoidal cells in its vicinity, whilst the passage of a sound into the frontal sinus will overcome any obstruction at the fronto-nasal opening. It is not always easy, or even possible, to pass a sound into the sinus, and in such cases some abnormality of anatomical configuration is in all probability the reason. The variation in the arrangement of the anterior ethmoidal cells is well known, and in many instances those that are grouped about the infundibulum may distort its usual shape and provide a considerable degree of obstruction. Cells actually in front of it, such as a lachrymal cell, may press backwards and render the passage S-shaped (fig. 5), or enlargement of the bulla ethmoidalis may press on it laterally

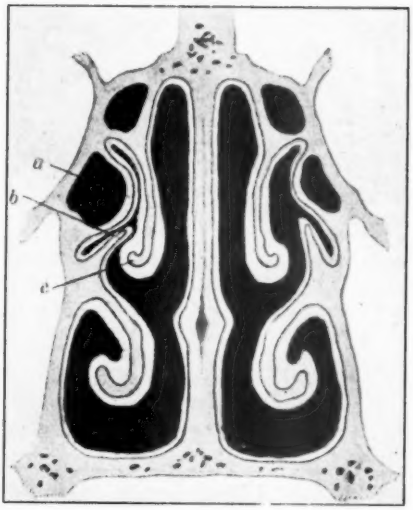

FIG. 5.—Enlarged bulla ethmoidalis.

(fig. 6). In these cases, which are not by any means rare, it will be necessary to remove the cells with a curette or biting forceps, so as to free the approach to the fronto-nasal opening and allow a sound to pass into the sinus (fig. 7). A large proportion of cases is cured by this procedure. The obstruction that prevents resolution of the sinusitis may be due to underlying ethmoiditis, and not only are drainage and aeration hindered, but ascending infection may be kept up, more particularly from the infundibular cells.

I believe that the frontal sinus and the anterior ethmoidal cells are nearly always simultaneously involved, and consequently any operation that is considered must be one which will drain both adequately. I am not much in favour of the stereotyped intranasal operation, along the lines suggested by Halle, Fletcher Ingals and others, but prefer to remove as much of the anterior part of the labyrinth as may be necessary, and to do this as thoroughly as possible, relying on subsequent sounding to effect a cure of the overlying sinusitis. The method of approach to the ethmoid

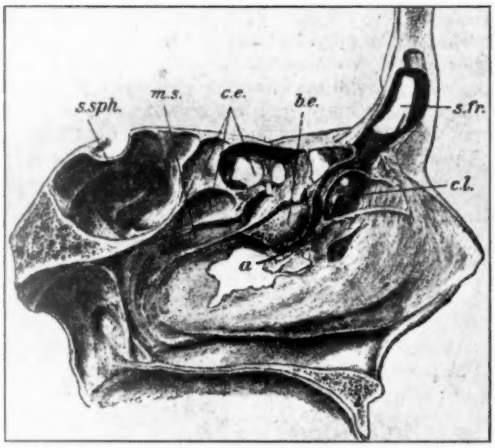

FIG. 6.—Shows tortuous fronto-nasal duct owing to enlarged bulla ethmoidalis and orbital-ethmoidal cell.

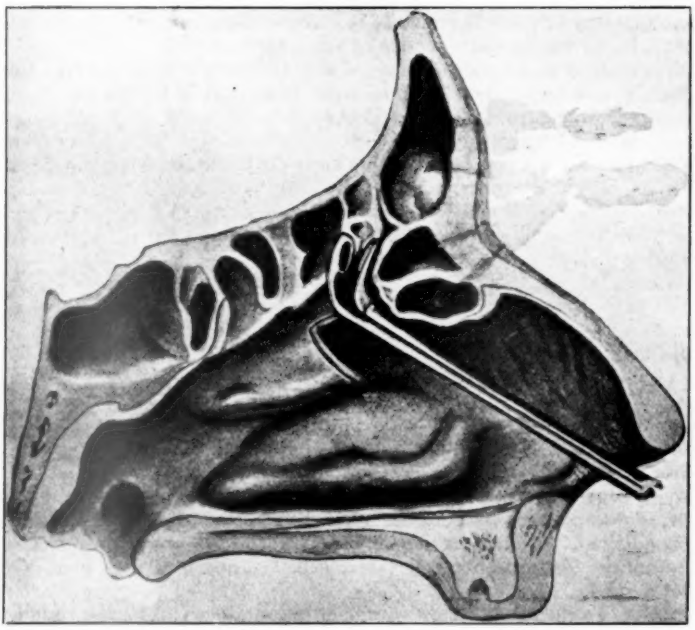

FIG. 7.—Shows disposition of cells round fronto-nasal duct and fronto-ethmoidal cell mounting up into floor of frontal sinus.

that I favour is that suggested by Mosher in which the point of attack is the cell of the agger nasi.

If the exenteration of the anterior cells is done satisfactorily there is above one simply the bony ring of the fronto-nasal opening. I know that in some cases the obliquity of the passage and the backward projection of the naso-frontal spur from the superior maxilla may interfere with the passage of sounds into the cavity and that one may be tempted to rasp away these offending obstructions. This temptation should be resisted for, although the immediate result may be satisfactory, as healing takes place and new bone is thrown out from the rasped surface, a higher degree of stenosis may occur than that which formerly obtained.

Although a large number of cases may be cured by these intranasal methods, a residue will remain in which the headache, tenderness, discharge, and eye symptoms persist. For these I believe some form of external operation to be necessary. Many years ago I gave up the Killian operation, not only on account of several unsatisfactory cases that I met with in Killian's clinic, but also because I came to the conclusion that the operation could not fulfil the object which it purposed to achieve, namely, the obliteration of the frontal sinus, without the deformity that the Riedel operation was bound to leave. Those who have had an extensive experience of the Killian operation will agree that in many of the cases, recurrence of headache, discharge, and polypus formation took place; Hajek, in Vienna, found himself compelled to re-operate on a large number of his own and other cases. In several he found a number of dead spaces filled with pus and separated from each other by fibrous septa.

It is nearly ten years since I suggested the method of external operation that is associated with my name. This is essentially a conservative operation and merely seeks to provide efficient drainage for the sinus into the nose whilst, at the same time, enabling the surgeon thoroughly to remove the ethmoidal disease which is so important a factor in the maintenance of sinus suppuration.

When operating on a series of cases of mucocele of the frontal sinus and ethmoid with which I was fortunate enough to meet, I was struck by the fact that in some cases the whole of the frontal sinus and the ethmoidal cells were converted into one large cavity lined with a modified mucous membrane, and that when this cavity was put into communication with the nose by means of a large opening, no further trouble occurred. It occurred to me that if, in suppurative cases, one could in some way imitate this natural method without unduly disturbing the mucous membrane, a similar result might be achieved. The operation that I suggested has this idea for its underlying principle.

The details of the operation are well known (figs. 8, 9, 10 and 11). By the removal of the whole floor of the sinus, including orbital galleries and extensions, and of the os planum of the ethmoid and the ethmoidal cells right up to the base of the skull, a single cavity can be created. The extent of this naturally depends on how far back it may be necessary to go in the ethmoid labyrinth to get beyond the diseased area. The drainage into the nose is arranged for by removal of a portion of the ascending process of the superior maxilla and of the nasal process of the frontal bone.

There is no set operation on the frontal sinus that is applicable to all conditions and it is not suggested that this operation can cure in every case, but I think that the method of approach is a good one and the operation can be modified to meet varying conditions. Increasing skill in its performance and an appreciation of the exact anatomical disposition of the area will, I think, lead to a high percentage of successful results.

As the *sine qua non* of the operation is free drainage from the cavity, naturally the maintenance of the patency of the new fronto-nasal duct is the chief concern.

In the majority of cases no difficulty arises, and retention of the rubber drainage tube for ten days and subsequent bougieing, with perhaps occasional touching of granulations with silver nitrate, is all that is necessary. There are, however, some cases in which the upper part of the nose seems very narrow and in which the

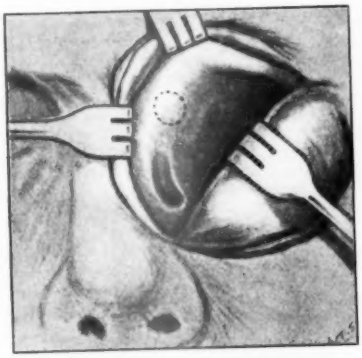

FIG. 8.—Howarth's operation (dotted circle shows where the frontal sinus is opened).

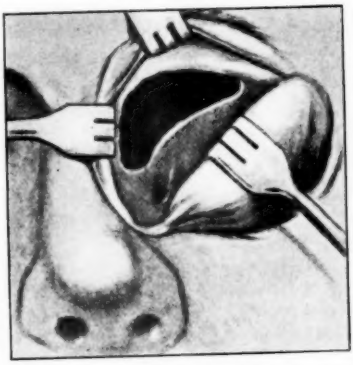

FIG. 9.—Howarth's operation. Floor of frontal sinus removed.

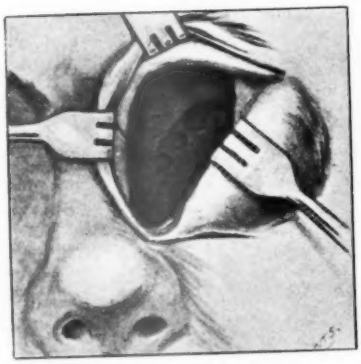

FIG. 10.—Howarth's operation. Floor of sinus and ethmoidal cells removed to base of skull.

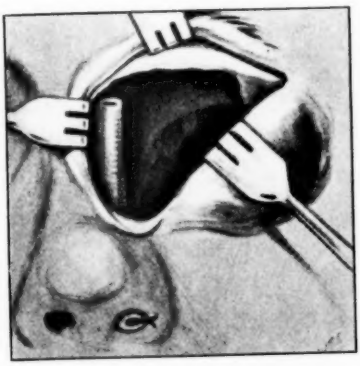

FIG. 11.—Howarth's operation. New fronto-nasal duct made and drainage tube inserted.

distance between the septum and the outer wall is very small so that the ultimate opening is more slit-like than one would wish to see. Again, in some cases the amount of granulation tissue thrown out from the cut bone, and the pressure of the

orbital contents may tend to produce a stenosis. In some cases I have covered the raw bony surface with skin grafts and this procedure may well be a useful addition to the ordinary technique, as it only takes a few minutes to accomplish, and may prevent the possibility of future stenosis.

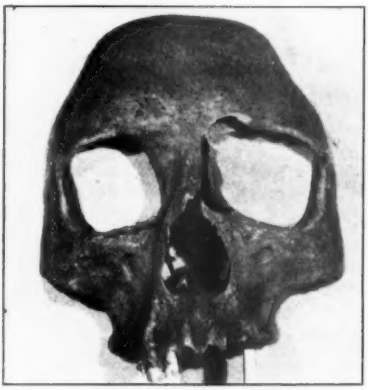

FIG. 12.—Howarth's operation. Black line shows extent of nasal process and frontal bone and ascending process of superior maxilla removed.

FIG. 13.—Howarth's operation. Reverse view of preceding specimens. Black line shows the nasal spur which projects backwards and which it is essential to remove.

The other important point in these difficult cases for which this operation is undertaken is the thorough removal of the ethmoidal disease that is invariably present. If this be not properly effected, re-infection of the cavity may take place and the ultimate cure be correspondingly delayed.

ILLUSTRATIVE CASES.

(I) A. S., male, aged 28. Right-sided nasal discharge many months. Pain over right eye intense for four weeks. Ethmoid disease with polypi. External operation April, 1928. Pus in sinus. Extensive involvement of ethmoid and also of right antrum.

(II) T. M., male. This man had a through-and-through wound in the late war, as a result of which both eyes were lost. It was not until seven years afterwards that the suppuration in the right frontal sinus appeared. There was considerable scarring in the ethmoids along the track of the operation. External frontal sinus operation November, 1925. Since operation patient has remained free from pain and discharge.

(III) F. W., male, aged 28, has had intense headache and nasal discharge. Septum operation and operations for removal of nasal polypi. Came to hospital with acute exacerbation and some external swelling. External operation 1928. No headache or discharge since.

(IV) H. G., male, aged 16. External swelling and pain. Extensive ethmoid disease. External operation April, 1930.

(V) R. J., female, nasal and post-nasal discharge for many months. Pain and occasional swelling externally. External operation January, 1925.

(VI) F. H., male, aged 48. Discharge from right side of nose and post-nasally for many months. Severe headache, increasing recently. Swelling of right eyelid intermittently since November. Now marked infiltration and œdema of right eyelid and forehead. Polypi and pus right middle turbinate region. External operation January 23, 1931. There was a large ragged hole in the floor of the frontal sinus. This was very extensive with numerous galleries. Ethmoid extensively diseased. External incision closed as usual at the end of operation. Œdema of eyelid and forehead settled down completely within a week.

(VII) S. B., male, aged 20. Operation for nasal polypi, right and left, two years ago. Now pus left side of nose. Small polypi. Pain and headache. Skiagram shows left sinus opaque. External operation five days ago (February 1). Very small thick-walled sinus full of pus. Most extensive ethmoidal disease necessitating complete removal of the ethmoidal labyrinth from front to back. Tiersch graft.

The President said he would like to have answers to the following questions: (1) Did acute frontal sinusitis occur without infection of the antrum? (2) Would not adequate treatment of the antrum obviate direct operation on the frontal sinus? (3) Assuming that a direct operation on the frontal sinus was necessary, was an obliteration operation possible? And, if possible, was it advisable? (4) What were the relative merits of the Howarth and the intubation methods? (5) In the experience of Members, did skin-grafting assist in maintaining drainage?

His own answer to the first question was No, excepting acute catarrhal frontal sinusitis. The answer to Question 2 came naturally as a corollary. Therefore the correct procedure in the treatment of acute recent suppuration in the frontal sinus was to treat the antrum first, drain that, and remove the anterior end of the middle turbinal. His answer to Question 3 was No. In some cases obliteration was physically almost impossible; and when it could be done it was highly undesirable. With regard to Question 4 his feeling was that the real problem to be solved in cases of frontal sinusitis was to find some means of draining the cavity adequately. With regard to the last question he had no experience and so would not express an opinion.

Mr. Harold Kisch, in answer to the President's first question, said that certainly frontal sinus suppuration could occur without antral infection. He had at present under treatment a case in which the antrum was clean and the frontal sinus was full of pus. Question 2 therefore did not arise. As to obliteration, he did not think so many obliteration operations would be tolerated in the South as appeared to have been performed in Edinburgh. His own results had been so good after

drainage that he felt that some free drainage method should be tried before submitting patients to an operation which led to considerable deformity. In regard to Question 4, he had not carried out the intubation method, neither had he done skin-grafting, as he had always felt it unwise to perform plastic operations in the presence of sepsis.

He had been pleased to see the cases shown by Mr. Negus (see p. 51), but he thought his own were cleaner. Skin-grafting in this region was still under trial, and it was necessary to wait and see the results. His own method of operation in frontal sinus cases was as follows and it was safe and easy: A small external incision was made running downwards from the supra-orbital notch, and the ascending process of the superior maxilla was exposed. All bleeding was stopped. He did not attempt to remove bone until the wound was dry; it was necessary to get a good view of the inside of the nose, and blood running down from outside obscured the view. He then removed the ascending process of the superior maxilla by four chisel cuts, so that the interior of the nose and the frontal sinus orifice were exposed immediately, or, if not, more bone was removed until the exposure was effected. Afterwards any ethmoidal disease was removed and care taken that the opening from the frontal sinus into the nose was free. The removal of the ascending process was the key to these operations; it was that which provided, by taking away of the anterior ethmoidal cells, the required drainage. Mr. Howarth removed the orbital plate of the ethmoid, but this he (the speaker) did not think necessary, because the ethmoidal cells could be seen and easily removed. He did not remove any of the floor of the frontal sinus, but the opening was made free by taking away more of the anterior wall.

His results had been very good; the drainage was so free that the patient could put a cannula into his own frontal sinus, and that was sufficient to cure the sinusitis; it was not necessary to remove mucous membrane. The scar was, in most cases, practically invisible.

The best way to make frontal sinus operations safe was (1) to check the hæmorrhage. He always used an injection of adrenalin and novocain externally, the interior of the nose being plugged and replugged under the anæsthetic, taking the adrenalin gauze high up in the nose. (2) To avoid the use of burrs, rasps, or curettes; removal was done by chisels or by forceps. (3) To avoid the use of rubber drainage tubes. Following his method, very little after-treatment was required. The sinus was washed out on the fourth day, and occasionally afterwards. Sometimes a bougie was passed to make certain that the way was free.

The stay in hospital after this operation was about a week, the patient being up and about on the fourth day.

Most of his acute frontal sinus cases were treated intranasally, but if it should be necessary to perform an external operation, the method described was a safe one, because the ascending process of the superior maxilla, a non-infected bone, was removed and there was little risk of spreading infection.

Mr. Musgrave Woodman said that some experiments on the frontal and other sinuses in animals had been carried out by Dr. Pickworth, Director of the Mental Research Laboratory, Hollymoor Asylum, and himself.

They had been performed on cats, and the general object was to demonstrate, (1) the direction of the lymphatic drainage from these sinuses, as shown by intra-vitam methods, and (2) the occurrence of an extension of a septic focus in these sinuses to the surrounding parts, especially the meninges.

The experiments were in two groups—(1) Aseptic injection with methylene blue and (2) Injection of organisms into the sinuses. In group A, the dye was placed aseptically into the frontal sinus by the intranasal route, without external damage

to the scalp or to the walls lining the sinus. As a result it was found that the dye remained in situ, and when the animal was killed fourteen days later, it was not appreciably altered. On the other hand, where damage or leakage had taken place into the scalp when the dye was placed into position by external operation, there was glandular involvement.

He now exhibited a specimen in which methylene blue had been placed in the frontal sinus by external operation, and a little leakage took place into the tissues of the scalp. The animal was killed on the fourteenth day, and the lymphatic glands beneath the jaw on both sides of the neck were seen to be stained deep blue in colour.

Another animal was inoculated by the intranasal route, and by misadventure the needle pricked the inner wall of the frontal sinus, and permitted the staining material to enter the meninges. The specimen he showed clearly illustrated the staining of the brain which resulted.

In group B several specimens were shown in which organisms, especially streptococci, had been inoculated into the frontal sinus. In each case, so long as there was no damage to the walls of the sinus, infection remained in statu quo. There was no extension into the meninges, or into the orbit, and no cellulitis of the scalp resulted.

The object of this group of experiments was to find out if there was any spontaneous migration of sepsis from the frontal sinus into the surrounding important areas.

[Mr. Musgrave Woodman showed seven specimens illustrating the experiments described.]

Mr. Herbert Tilley said that Mr. Harmer's method was new in technical details, but the general principle of the operation was the same which Dr. Lambert Lack introduced at the Golden Square Hospital, London, and he (the speaker) remembered that many patients could be seen walking about the ward with a little lead "style," the upper end of which projected from the inner end of the external wound. The "style" was kept in for weeks or even months, until it was surrounded by granulation tissue, and then removed.

There was a risk in every radical frontal sinus operation, and in advising it one assumed a definite responsibility. The only point he criticized in Mr. Harmer's operation was the long time during which many of these patients had to go about wearing a sign-manual of the surgeon's handiwork; this might be objected to by many sensitive patients.

In answer to the President's first question, he thought that inflammation, in its initial stages, must involve simultaneous infection of all the sinuses. Still, one might often find a residual frontal sinus suppuration when the antral infection had spontaneously recovered. In the same way, sometimes an acute frontal sinus suppuration would subside without surgical intervention. When the external radical operation had been performed and the mucous membrane removed it was six weeks before the patient was cured by complete obliteration of the cavity of the sinus by granulation tissue. Nowadays the mucous membrane was not removed, but left to recover by establishing free internal drainage into the nasal cavity. As one of the early pioneers in the surgery of the frontal sinus, he would like to impress on the junior members of the Section the importance of bearing in mind that in every frontal sinus operation, the "key situation" was the ethmoid region, because the cross-roads of all the sinuses met there, and if these were obstructed, one would never get the good result hoped for in operations on any individual sinus. If the ethmoid region was effectively treated, whether the operation on the frontal sinus was a Howarth, Killian, Ogston-Luc, or any other, a more speedy and good result would be effected on the frontal sinus. A thoroughly efficient drainage of the antero-ethmoidal cells and enlargement of the fronto-nasal canal would frequently

be followed, in a longer or shorter time, by cessation of chronic suppuration of the frontal sinus without any radical operation on this air cell. In his (Mr. Tilley's) younger days many of his patients had refused the external operation he had advised, and now they came occasionally only for the solace of an optimistic report. It was interesting to notice that in many cases the discharge had entirely ceased, in the course of time, while in others there was still some slight suppuration, but not enough to cause either local or distal symptoms of any consequence.

[Mr. Tilley then showed slides illustrating the intranasal and external operations on the frontal sinus. One of these was a skiagram of an acutely inflamed sinus in which a zone of inflamed diplœic cells formed the upper boundary of the cavity. To curette such an area would risk exposing it to sepsis with the possible complications of osteomyelitis—often a fatal accident.]

Sir James Dundas-Grant said that the first case at the first meeting of the Laryngological Society, in 1893, was one of empyema of the frontal sinus, brought forward by him, and it seemed to have been dealt with by a mixture of the operations which had been described to-day (*Proceedings of the Laryngological Society of London*, 1893, i, 1). The introduction of a drainage tube, and its maintenance in position for a considerable time, helped greatly in arriving at a good result.

With regard to acute frontal sinusitis, people who were frantic with the pain were sometimes immediately relieved by the removal of the anterior part of the middle turbinated body. He had seen some antrum cases which had cleared up or been cured after one or two irrigations. It was likely that the affection of the antrum which had been cured so quickly had been due to a secondary flow of secretions from the inflamed frontal sinus which, from its vertical position, might have undergone spontaneous cure.

He (the speaker) had shown before the Section some cases of Killian's operation which answered very well. In one such case the disease was bilateral. He had removed a good deal of the ascending process on both sides, and the patient wore tight pince-nez, which he, the speaker, thought were going to be a trouble, but did not prove so, in spite of the removal of large portions of the ascending processes.

All types of operation had their advantages, and in a few of his own recent cases he had used what might be described as a combination of the methods advised by Mr. Harmer, Mr. Howarth and Mr. Kisch respectively.

Mr. Negus had shown cases which had done well after skin-grafting. Had Mr. Negus thought of a mucous membrane graft? He (the speaker) remembered Mr. Tilley's proposing at a meeting of the Section to carry out skin-grafting of the frontal sinus and he, Sir James, had feared that the procedure might encourage the development of cholesteatoma. The operative procedure adopted in any particular case should be decided upon what was found.

Mr. T. B. Layton: May I classify frontal sinusitis thus?

I.—Sinusitis with orbital or intracranial symptoms: (*a*) Acute, (*b*) chronic, secondary to either (1) frontal sinus or (2) ethmoidal cells.

II.—Frontal sinusitis without such sequelæ: (*a*) Acute, (1) catarrhal, (2) suppurative. (*b*) Chronic, (1) suppurative, (2) with polypi.

It seems to me just as unpractical to discuss all these different conditions at one time as it would be to discuss acute otitis media and mastoiditis, chronic ear discharge with or without disease of the bone, jugular thrombosis, cerebral abscess and cholesteatoma, all at the same time. My remarks, therefore, refer only to cases that come under II—(*a*) 1 and 2, and (*b*) 1, which I believe are different stages of the same disorder.

My conception of frontal sinusitis is that of Mr. Howarth when he says that "the frontal sinus and the anterior ethmoidal cells are nearly always simultaneously involved"; but I should like to express it differently.

At the upper end of the primitive semilunar groove there are in the new-born infant some four frontal recesses (Parsons Schaeffer) which develop into ethmoidal cells, and these enlarge forwards and upwards to the angle at the junction of the nose and the cranial cavity. One of these passes on to expand the vertical portion of the frontal bone.

It is an inflammation of all these flask-shaped cells which constitutes frontal sinusitis, and this should be considered as a clinical and not as an anatomical entity. If this concept of frontal sinusitis be held, then an inflammation of those other round cells that open under the middle turbinal constitutes an anterior ethmoiditis.

What then is an acute frontal sinusitis? For a paper such as that which Mr. Fraser and Dr. Stewart have put before us, six months is a very useful date to take as the limit between the two; but when the case is before one the difference is one of clinical signs rather than of date, and many cases may be said to have reached the chronic stage before the six months are up.

Now I do not believe that except under the rarest conditions should any set operation, external or internal, be done in a case of acute frontal sinusitis. So rare are these conditions that I have yet to meet the case. I further believe that in every instance *there is greater danger to the life of the patient from the operation than from the disease.*

The only operative treatment that I employ is very gently to wash out the maxillary sinus, which is usually also involved, with a view to removing the larger amount of the pus that is poisoning the patient. The only other thing that I will consider is the high resection of the middle turbinal; but nowadays I believe even this to be so dangerous that I am loth to employ it.

To my mind the treatment of chronic sinusitis depends upon two characteristics of the nasal mucous membrane—its stupendous power of swelling up when it is irritated, and its extraordinary power of recovery when the cause of that irritation is removed. Now in chronic sinusitis that cause of irritation is the pus poured into the nose either from some other sinus or from the affected one under discussion.

An anatomical point which is but little recognized is the fact that all the openings into the middle meatus can be covered by a shilling and probably by a sixpenny piece; therefore, pus poured into the nose from the maxillary sinus will so cause swelling of the mucous membrane around the openings of the other sinuses that it is the presence of the maxillary sinusitis which prevents the frontal sinusitis from getting well.

The first treatment of frontal sinusitis is, therefore, the treatment of the maxillary sinus by repeated puncture and lavage, or if this fails, by some operation that will divert the pus from the middle meatus to the inferior one. In the majority of cases this will result in the mucous membrane of the middle meatus becoming so much less swollen that the pus can drain away from the cells involved in frontal sinusitis, and no other operative treatment should be attempted until this has been done.

Where this fails, or in the unusual case in which frontal sinusitis is unaccompanied by maxillary sinusitis, the two operations to be considered are the high operation on the deviated septum and the high resection of the middle turbinal. I am not sure even now which is the more important, but of this I am sure—that it is of the utmost importance in each case to decide which is the right one to do. It is an error of judgment on this point which leads to failure and becomes the precursor of the external operation. It is important to remember that the septum must be straightened first or not at all. If interference with the structures of the middle meatus fails to cure the condition before the operation on the septum, it is not

likely that this operation will subsequently be of value. This principle is well illustrated in the second of the three cases shown by Mr. Negus (see p. 51) to-day.

So far as I have gone it is probable that I am in agreement with the practice both of Mr. Howarth and of Mr. Fraser, but I now want to break a lance with them, for, from their description, I do not believe that either of them does the true high resection of the middle turbinal. And yet this is the most important operation for an inflammation in any of the cells that open into the middle meatus other than the maxillary sinus. Hajek goes so far as to say that the operation is the precursor of an accurate diagnosis in the majority of cases of frontal sinusitis.

It is the piece of bone attached to the lateral wall of the nose immediately behind the upper end of the anterior margin that needs removal. When Mr. Howarth says he removes "the anterior end of the middle turbinate" I doubt whether he gets the right piece, and Mr. Fraser is certainly full of false doctrine when he talks about removing "the anterior end and lower border of" this structure.

When these things are done there are few cases of frontal sinusitis that do not recover, but there are still those other minor intranasal operations such as opening an agger or other anterior ethmoidal cell or biting away a piece of the bulla or of the uncinate process in order more fully to secure drainage in the region of the opening of the fronto-nasal duct. It is only when these have failed that the external operation on the frontal sinus should be done.

Holding, as I do, these views, my hearers will understand the pain with which I have heard of the new operation that has been described to-day. I have done four external frontal operations for sinusitis in twelve years, the advocates of this operation have done fifty-four in ten. But even if an external operation is necessary this one seems to fail in the primary principle of all external frontal sinus operations. This is that no variety will be of use unless free drainage is secured down into the nose. It is the basis of Mr. Howarth's operation, but the description of this new operation does not suggest that such free drainage is necessarily obtained, and it may be that the "number of failures" can be attributed to this rather than to the non-attendance in the out-patient room.

Lastly, may we have an explanation of the pathology of the condition that is labelled "vacuum sinusitis"?

Mr. W. Ibbotson said that up to ten years ago he had been very much disappointed with most of his results in cases of frontal sinusitis, and had come to the conclusion that he must have been committing some gross error or omitting an important procedure when he found that pain and discharge, though very much relieved by operation, still recurred from time to time. He decided that this was most likely due to his omitting to treat the original source of infection, which, in most cases at any rate, would seem to be in the pharynx. For about the last ten years, however, he had been performing a two-stage operation, and his results had been infinitely more encouraging. The first stage consisted in free external drainage, leaving the wound entirely open, and treating it with non-irritating antiseptics. The second stage was employed for the plastic repair of the wound, and the performance of tonsillectomy. He considered this tonsillectomy (when the tonsils were definitely infected) to be most important, and also largely responsible for the healing by first intention that had been the rule in the majority of his cases. The same rule, he believed, should apply in the operative treatment of mastoid suppuration, and it was very instructive to note that, in many of these cases, he had found that the homolateral tonsil was the more extensively diseased.

Dr. P. Watson-Williams said that we had still something to learn in striving for ideal methods of dealing with these cases.

Within the first of the President's questions lay the clue to some of the problems under discussion. He agreed with Mr. Tilley that from the strictly pathological standpoint, acute frontal sinus disease never occurred without antral infection, since acute infective rhinitis always involved the sinuses, but usually followed the common course of these infected conditions in spontaneous recovery. Clinically, however, the term "sinusitis" meant a sinus infection which caused untoward symptoms of special character, and in that sense acute frontal sinusitis often occurred without antral infection. In most cases the determining cause of frontal sinusitis was inefficient drainage or actual obstruction to it, due often to involvement of ethmoid cells or the arrangement of those cells and so forth. Hence the key-note to success in treatment lay in the removal of the obstruction in the fronto-nasal duct.

The essential difference in the various operations advocated was that radical operations sought to obliterate the sinus cavity and involved the removal of the mucosa and of the anterior wall: whereas conservative operations aimed at establishing drainage, but not at obliteration of the cavity.

In both forms of procedure the chief aim was complete exenteration of the anterior ethmoidal cells and the agger cells and removal of the fronto-nasal spur. The general tendency was to rely as far as possible on conservative methods, whether by "external approach," as in Mr. Harmer's and Mr. Russell's prolonged tubage or Mr. Howarth's operation, or by the "per-nasal operation."

Mr. Howarth had warned operators against the removal of the fronto-nasal spur by the per nasal method, because "it would result in the bone reproducing itself and making the stenosis worse than when one started." Yet Mr. Howarth removed it through an external opening, and he (the speaker) did not think that either Mr. Howarth or himself had, in many hundreds of cases, experienced any thickening or reproduction of the bone following its operative removal; it might therefore be no more than surmise.

In acute sinus trouble the great thing was to rely on palliative measures, as there was a tendency to spontaneous recovery. In the acute cases it had been his habit to avoid anything in the nature of an intranasal operation during the acute stage, i.e., until the patient had had the opportunity of developing some local tissue resistance.

He had been interested in Mr. Fraser's results, because he had employed the intranasal method in some acute cases, and in only one did erysipelas result and in another case, scarlatina, and all his patients had recovered. On attacking this region by operation in the acute stage there was some risk of systemic invasion. He would rather trephine the floor of the sinus (after external incision) to relieve tension.

At a special discussion held by the Section in 1914[1] on the "Intranasal operative treatment for Frontal Sinusitis," he had described his own technique very fully and had not since found any cause for wavering on the subject from the line he took then, except that he now relied on a special rasp for removing the naso-frontal spur, thus immensely simplifying the operation and avoiding any need for the rotating burrs, chisels, or back-cutting forceps formerly employed. For attacking agger cells he preferred his own method of entry which he demonstrated on the screen, to that which Mosher introduced. Having removed the ethmoid cells, he passed the rasp up into the frontal sinus very gently, and the rasp would usually enter merely by its own weight. He rasped away the fronto-nasal spur, and the little hook at the top prevented the rasp slipping out during the forcible

[1] *Proc. Roy. Soc. Med.*, vii, 7, p. 121 *et seq.*

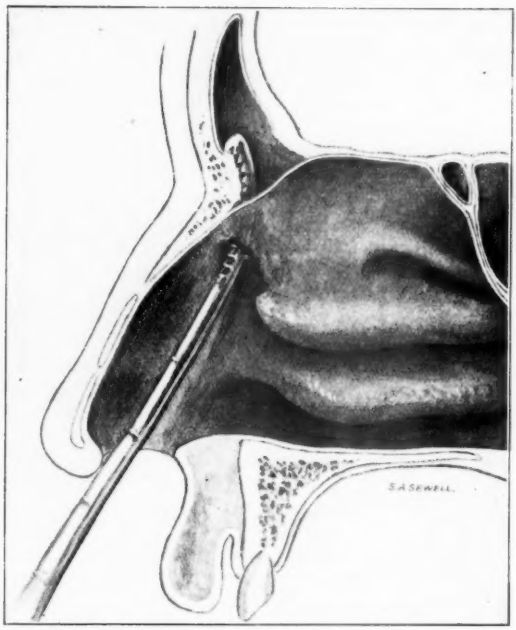

FIG. 1.—Intranasal frontal sinus operation (2nd stage), i.e., after removal of the agger and other ethmoidal cells. The rasp is shown at the bottom of its downward excursion cutting away the nasal crest.

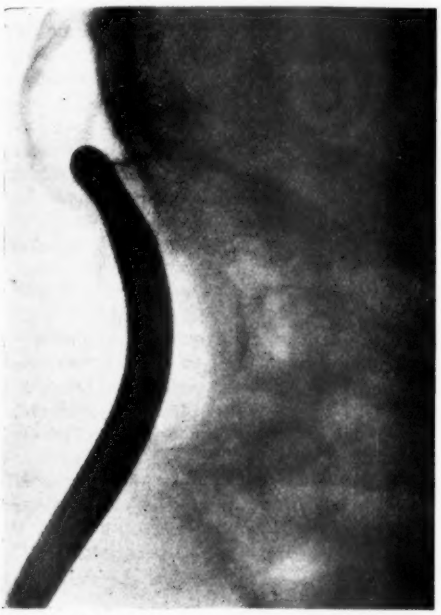

FIG. 2.—Intranasal frontal sinus operation. Skiagram showing that the removal of naso-frontal spur and anterior ethmoidal cells affords good drainage, as it allows the large bougie (18 mm. in circumference) to enter the frontal sinus.

downward rasping, and thus avoided the risk of injuring the mucous membrane. In the majority of cases one could get good permanent drainage in this way (fig. 2), and the results were highly satisfactory.

Sir StClair Thomson said that his answer to the President's first question was "No, never." Antral invasion was always associated with acute frontal sinusitis. It might clear up first, leaving the frontal sinus suppuration persistent. That was all the more reason for treating the antrum by puncture and lavage in all these cases.

In answer to Question 2: Obliteration of the frontal sinus was possible, but not of the fronto-ethmoidal cells. In the cases in which one re-opened and found granulation tissue and pus, he thought this came from the fronto-ethmoidal cells. These frontal sinuses were frequently re-opened and found not to have been obliterated. A French writer had said that there was nothing new except what had been forgotten. If one looked at the publications of Luc in the last century, and the work of Fletcher Ingals in the early part of this, it would be seen that the principle of intubation and drainage differed little from those now described.

Intranasal operation was rarely necessary in acute sinusitis. Surely it was running a grave danger in acute cases, to operate on the middle turbinal and open up the lymphatic spaces which surrounded the fine ends of the olfactory nerve.

Mr. J. S. Fraser, in reply, said he was sorry that so little had been said in the discussion about the fatalities in frontal sinusitis.

To illustrate the fact that one easily forgets one's bad results he might mention that when he thought of bringing the subject before the Section he had said to Dr. Logan Turner "I do not think I have ever had a fatality as a result of operation on the frontal sinus," and Dr. Turner had replied "Oh yes, you have," and had then instanced a case.

Mr. Tilley had asked how long it was necessary to wait for obliteration. There was no need to wait, the obliteration cases which were successful were successful right away. All mucous membrane was removed and the sinus was packed with iodoform gauze at the operation. This gauze was removed through the nose two days later and the posterior surface of the periosteum was brought into contact with the posterior wall of the sinus and pressure applied with gauze, wool and bandage. There was thus complete obliteration. The resulting deformity depended on the depth and extent of the sinus. He pleaded guilty to having done rather more "obliteration" operations than he cared to look back upon. He and his colleague had confessed in the paper that in the future they would try the Howarth operation more frequently, and would only resort to the obliteration operation when the Howarth operation was not successful.

Mr. Layton was doubtful if he (the speaker) removed the anterior end of the middle turbinal. He could only say that he tried to remove the anterior part of the middle turbinal and open up the agger cells as completely as possible.

In reply to the President, he was sure that there were many acute cases in which the frontal sinus was affected but the antrum was free from sinusitis; such cases had been proved by negative results of puncturing the antrum.

Mr. Douglas Harmer, in reply, said that what impressed laryngologists was the danger in these cases. In acute sinusitis there might be severe swelling, œdema, proptosis, tenderness of the brow, rigors, and a high temperature. The condition was as dangerous as an acute appendicitis and one could not always relieve it by puncturing the antrum or by any intranasal treatment. In such a case an external operation must be performed in order to save life, but he agreed that one must be careful when advising such a radical operation.

It had been hinted that his operation had been described many times before but his search through the literature had shown him that all the previous operations had been essentially different. In these the passages into the nose had been made either by a burr or gouge, the lining of the ducts being thereby removed or destroyed. The essential condition of his method was the dilatation of the duct without damaging its lining. If the constriction was very severe the surgeon might not be able to pull the tube through the duct without damage to the membrane and in such a case he should simply pass a thread through it and leave it for a few days before attempting intubation.

With regard to chronic sinusitis: some people became more and more ill in spite of intranasal surgery. Their pain could not always be relieved by it; the general nervous condition sometimes became very serious. In such cases some type of radical operation was a necessity. He believed that intubation caused far less shock and was less dangerous than a radical operation. With the latter, complications occasionally occurred. There might be a spread of inflammation necessitating further operations, and instead of the patient being in bed for a week, he might be laid up for the greater part of a year.

He had been asked whether there was such a thing as "vacuum sinusitis." He was sure that there was. The condition was due to great constriction of the frontal duct and the acute pain was caused by a vasomotor swelling of the lining membrane, which might occur quite suddenly and close the duct. In such a case, on opening the frontal sinus, one might find its lining greatly retracted and it might be very difficult to pass even the finest probe through the duct into the nose.

With regard to the ethmoidal cells; in nearly all the cases described, intranasal surgery had been tried and the ethmoidal cells treated before the external operations were advised.

Mr. Walter Howarth, in reply to Mr. Layton, said he thought that he removed the anterior end of the middle turbinate completely by the use of Sluder's knife. Dealing with Dr. Watson-Williams' remarks about the removal of the nasal spur, he quite agreed that this was important but thought that only a small portion of it could be safely removed by the intranasal method, whereas by the external route the whole bone could be got rid of from front to back. He did not like rasping the bone, with the consequent creation of a raw surface.

Sir StClair Thomson had said that there was nothing new in these operations. He certainly thought that Mr. Harmer's procedure embodied a new feature in the progressive dilatation. As regarded his own operation, the removal of the nasal process of the frontal bone and the ascending process of the superior maxilla to bring the drainage further forward had not been suggested by anyone hitherto and differed considerably from Killian's procedure. The retention of the lining mucosa was also new.

Two Cases of Multiple Nasal Sinusitis.—HAROLD KISCH, F.R.C.S.

(I) Mrs. M. attended at the hospital with a long history of nasal suppuration. The whole of the nasal sinuses have been drained, the frontal sinuses by external antrum operation, the antra by a modified Caldwell-Luc operation.

(II) Miss T. had right frontal and antrum sinusitis, following typhoid fever. She has had an external frontal sinus operation, and modified Caldwell-Luc antrum operation. She also had a chronic mastoiditis, and this was treated by insertion of a temporal muscle graft.

Three Cases showing results of External Frontal Sinus Operation combined with Skin Grafting.—V. E. NEGUS, M.S., F.R.C.S.

All operated on by Howarth's method, with the addition of a skin graft applied to the orbital periosteum to prevent subsequent narrowing of the new fronto-nasal opening, as employed by Professor Seiffert in Professor von Eicken's clinic.

Free opening in each case without any dilatation after operation.

(I) Female, aged 35. Recurring swelling and pain over left eye for seven months prior to April, 1929, when she attended King's College Hospital with acute frontal sinusitis; red, tender fluctuating swelling over left sinus with temperature of 100°. Left antrum opaque on transillumination.

2.5.29.—Howarth's operation and intranasal antrostomy on left side. 13.5.29.—Skin graft applied to orbital periosteum. No subsequent dilatation.

Pus continued to discharge from left side of nose, but by January, 1930, antrum was clear and from the frontal sinus only a few flakes of muco-pus were washed out.

Patient is now quite well, without pain and with very little discharge. The fronto-nasal canal is freely open, but there are a few granulations at its nasal orifice.

(II) Male, aged 31. Nose operated on and tonsils cut in 1919, because of frequent colds. Pain appeared over right eye in 1921, and continued in spite of medical treatment and attention to teeth and eyes.

In 1925, right antrum contained pus and was washed out ten times without improvement; symptoms continued intermittently until 1929 in periodical attacks, causing the patient to wake with severe pain, with tenderness over the right frontal sinus.

Ethmoidectomy and partial turbinectomy in January, 1929, and submucous resection in June, 1929, without improvement. In November, 1929, external operation with skin graft to orbital periosteum.

Short attacks of slight pain in April, 1930, but none since. Patient still has some thick discharge, but feels well and can play games.

(III) Female, aged 54. Severe pain in region of left frontal sinus two and a half years ago, with much swelling at times above left eye. Intranasal operation two and a half years ago, and in December, 1929, without improvement. Great pain in May, 1930, necessitating external operation, with tube in nostril for three weeks. No improvement.

First seen by exhibitor in October, 1930, with severe pain over sinus and on top of head on left side. Right antrum infected; left fronto-nasal duct quite impassable.

27.10.30.—External operation, with skin graft; no subsequent dilatation.

Fronto-nasal opening is now freely open; there is a little muco-pus on lavage.

Patient still suffers from much nasal discharge, but the original pain is gone, and only occasional pain of a different type, described as "a cold feeling," is noticed.

An Unusual Case of Frontal Sinusitis.—WILLIAM IBBOTSON, F.R.C.S.Ed.

Male, aged 39, first seen, 28.3.30.

History.—Left-sided nasal discharge, yellow, non-offensive. Occasional epistaxis (left). Smell diminished; no obstruction; constant left frontal headaches; impaired general health; "nerves," anorexia; disturbed sleep; loss of weight. No night-sweats; slight cough. Left intranasal frontal sinusotomy 1912. No cessation of discharge afterwards. Two years ago an abscess broke out just medial to the left internal canthus; this closed and reopened four or five times and is still discharging; no radiography had been carried out. Patient has one healthy child. No important family history.

On examination.—Chronic suppurative left frontal, ethmoidal and maxillary sinusitis, confirmed by radiography. Definitely infected tonsils, especially left; two infected teeth in left side of mandible.

Diagnosis.—The suppurating facial sinus together with the history, etc., strongly suggests tuberculosis of the affected sinuses. In my opinion the dental and tonsillar lesions also play an important ætiological part. The condition of neurasthenia that is present may, I think, justly be called "toxic neurasthenia," seeing that it is very largely dependent upon the above lesions.

Treatment.—Dental.

Examination of chest, April, 1930.—Active tuberculosis in both lungs, with positive sputum. Sent to a sanatorium.

21.8.30.—Lungs healed. Negative sputum. Gaining weight. Suppurating facial sinus still open and active. Nasal sinusitis not diminished.

Operation.—Stage 1. 3.9.30. Left conservative external frontal and intranasal ethmoidal and maxillary sinusotomy. No suturing. Anæsthetic: intratracheal chloroform.

Stage 2. 13.9.30. Complete suturing; wound treated with "bipp." Tonsillectomy by dissection. Anæsthetic: intratracheal chloroform.

February, 1931.—Recovery was gradual, but pronounced. The wound is well healed, with very little disfigurement, and the discharging facial sinus has long since closed. There is still slight maxillary and ethmoidal suppuration, but its character is much more mucoid. General health good; weight steady; patient is carrying on with his work and there are now no signs of neurasthenia.

Remarks.—Unfortunately, I did not obtain a microscopical report on the nasal sinusitis. My own belief is that this successful result was due to the following factors: (1) complete pulmonary recovery before any operation was attempted; (2) performance of the operation in two stages, so as to give the frontal sinus time to recover before closing it over; (3) removal of the dental and tonsillar lesions, especially the latter. This, to my mind, is a point of the utmost importance.

Section of Ophthalmology.

[*January* 9, 1931.]

Marginal Degeneration of the Cornea.—J. H. DOGGART, F.R.C.S.

Patient, male, aged 21, has had failure of vision in the left eye for a year, during which he has had several attacks of mild conjunctivitis. There is a marginal opacity of the left cornea, extending from 8 o'clock to 2 o'clock. This opacity is vascularized by vessels running inwards, in a radial direction, and the vessels are sharply limited by a sinuous white line. This is a very early case of marginal degeneration, not having yet reached the stage of furrow-formation. In a few years' time there will probably be a good deal of thinning in the cornea, and still later there will probably be ectasia. The best vision obtainable is $\frac{6}{9}$ in the left eye, with minus 1 sphere, plus 2 cylinder, at an axis of 30°. This astigmatism is typical of the disease.

[I have to thank Mr. Duke Elder for permission to show the case.]

Discussion.—Sir RICHARD CRUISE said that this did not appear to him to be a degenerative condition but, rather, a sluggish form of sub-epithelial infiltration from an infective source. He had seen this condition with finger-like projections invading the cornea, in other cases of sluggish formation.

Mr. M. S. MAYOU said that, as there was no ectasia, he regarded this as a congenital condition, and thought the increased vascularity was due to the conjunctivitis from which the patient had suffered.

Conjunctivitis.—O. GAYER MORGAN, F.R.C.S.

I first showed this patient in February, 1930, as a case of ? Parinaud's conjunctivitis. It is interesting that so many of these cases turn out to be tuberculous on further investigation. In March, after a further examination of sections of the granulations, and after injections had been made into a guinea-pig, the condition was found to be definitely tuberculous. There were very marked cock's-comb granulations in the lower fornix and enlarged solitary follicles over the tarsal plate. There was also a very large pre-auricular gland, and a gland under the angle of the jaw. Since March, 1930, the patient has had treatment by the carbon arc-lamp, beginning with one minute twice weekly. This was continued for four months; then it was increased to 1½ minutes at a time, then to 2 minutes; and now he is having 2½ minutes twice a week. He has improved steadily, and now there is little to be seen in the lower fornix. The solitary follicles have disappeared, the gland, which was large and soft, is now much smaller and hard, and I think one can say that the tuberculous focus has been eradicated. The method employed was eversion of the lower lid and protection of the upper lid and eye by dental stent and then eversion of the upper lid and protection of the lower. There has been no corneal irritation during the treatment

Discussion.—Mr. C. L. GIMBLETT said that he had had a case similar to that just described by Mr. Morgan, with an enlarged pre-auricular gland. He removed a small piece of the granulation from the lid, and the report on it was that there were no giant cells, but there was a vast excess of lymphocytes. That case was diagnosed, by several who saw it, as the Parinaud condition. The gland in front of the ear was soft, and the skin over it was typical of what was seen over a breaking-down tuberculous gland. His own case had been treated with tuberculin. The gland broke down and discharged, then healed completely, and the conjunctival condition also subsided, so that the conjunctiva was now normal. There was now a healed, healthy scar in front of the ear, but all had been in a state of quietude for three months.

Mr. J. H. FISHER asked whether this was an infection with bovine tuberculosis or with human tubercle bacillus. The ordinary case of cervical gland tuberculosis in childhood was bovine; the infection having taken place through the nasopharyngeal mucous membrane, the initial lesion was rarely seen. It would be an interesting observation, when these ophthalmic cases were encountered and the primary lesion was obvious, to discover whether the infection was with bovine or human tuberculosis.

Mr. P. G. DOYNE said that he had had three examples of this condition shown to the Section. All three had the same ætiology; they were definitely caused by a scratch of the conjunctiva with a finger nail. All had an enlarged pre-auricular gland and were true to type.

Colour-blindness in a Woman, aged 20.—F. E. PRESTON, D.O.M.S.

I have shown this case of colour-blindness, not so much as a rarity (though the percentage of females who are colour-blind is small, i.e., about 4%, whereas the percentage of males is about 10), but to raise a practical question. Hitherto, colour-blindness has only concerned those who have investigated the cause of this defect, or those who have had to examine men for the railway, the marine, and other services. With the advent of coloured lights to signal motor traffic, it will soon concern all of us, pedestrians and motorists. I examined a friend of mine by the Ishihara test and found that he was a trichromic. Then I examined him by the Edridge green-card test, and found he was dangerously colour-blind. Next, I examined him in the fog on a railway signal, and all his answers were correct, even at a considerable distance.

In view of this, I should be glad if anyone could suggest a simple, inexpensive test to distinguish dangerous from non-dangerous colour-blind people. Are not the present tests too severe where it is only a matter of distinguishing red from green? The percentage of young children with defective colour-vision seems to me to be much the same in both sexes, whereas in adults it is twenty times more common in males than in females. It seems that to some extent colour vision is educative; girls are taught to take an interest in the colour of their dress, but boys are not. If colour-vision is educatable, why not educate it in schools, seeing it is a necessary thing in our everyday life?

Extraction with Conjunctival Bridge.

By NORMAN FLEMING, M.B.

FOR about two years I have been operating on my cataract cases by a method differing in certain respects from that generally practised, and the results have afforded me so great satisfaction that I would like to put the details before others for their consideration. As it is not easy to express details of this kind so as to leave no room for misunderstanding, I decided to have a cinematograph film made of a few cases, and, if successful, allow it to do the talking for me. Considering the technical difficulties of taking such a film, and the very disturbing nature of a cinematograph camera as an accompaniment to the extraction of cataract, I am fairly satisfied with the result.

There are various points to which I would like to draw attention. With regard to the preliminary irrigation, I clean out both fornices with swabs mounted on Indian sticks, in a stream of saline: this, I find, removes any mucus that may be present and aids in the general cleansing by opening up all folds in the conjunctiva to be flushed by the running water; it also avoids any touching of the palpebral conjunctiva when everting the upper lid.

The next step is the opening of the lens capsule by a slightly curved vertical incision with a Ziegler knife; no loss of aqueous need result from this.

The Graefe section follows, with entry at the same point, and differs from the usual procedure in that, when cutting upwards, it is caused to include a broad band of conjunctiva, the knife coming out above just deep to this membrane and dividing it in an upward direction by two parallel cuts about six millimetres in length; the knife is then withdrawn from under the bridge.

Next follows the removal of the lens. An iris repositor, with the end bent to an angle of ninety degrees, is introduced under the bridge and the lens pressed slightly

downwards by a stroking movement on the sclerotic; it is retained in this position while a curette is applied to the cornea to make the lens present in the usual manner. As soon as the lens presents, the iris repositor is discarded, and a needle is pushed into the lowest available part of the periphery of the lens on one or other side, and with this the lens is rotated out of the eye without further pressure. The iris usually falls back into place and the use of a repositor is rarely necessary. Any remaining lens matter is washed out if desired and the operation is completed. I use the Madras bandage. For demonstration of the use of this particular bandage and the method of preliminary irrigation I am indebted to Colonel Kirkpatrick, with whom I had the privilege of working in Madras in 1919.

Extraction with a conjunctival bridge was first described by Desmarres about 1870 and has been carried out by various surgeons since that time, but it has never been my good fortune to see anyone else perform the operation.

It will be generally conceded that, provided it is successful, cataract extraction without iridectomy gives the best result, and I have found, so far, that bridge extraction, by fixing the lips of the wound and rapid healing, offers a safeguard against prolapse which justifies the omission of an iridectomy. If for any reason it is desired to perform iridectomy, it can readily be done, and, as a routine, can be facilitated by fashioning the bridge somewhat to one side as recommended by Mr. Leslie Paton.

With regard to results: When all goes well, it may require careful examination to see that the eye has been operated on at all, in which case, unless any remaining capsule or fundus trouble is present, $\frac{6}{6}$ vision may be expected. The bridge holds the cut surfaces in perfect apposition and the wound heals surprisingly quickly with very little reaction or resulting astigmatism. Amongst the last eighteen cases in which I have operated I have had one failure. The patient was a decrepit old woman who developed panophthalmitis within two days of the operation, in spite of a sterile culture; presumably this was a case of endogenous infection. One woman vomited frequently during the first twenty-four hours following operation and had a double prolapse, one on either side of the bridge; the final result was satisfactory. A third patient, an old man, got out of bed, took off his bandages and went into the garden on the sixth day; according to him, he never touched his eye, but he returned with the anterior chamber full of blood. This cleared up and left him with a good eye but a slightly eccentric pupil. The other cases presented no abnormality.

Discussion.—Mr. F. W. Law said he had assisted with some of these operations. The opinion he had formed was that it was a delightful procedure when everything went straightforwardly, but that with a "sticky" lens or other complication it was a disadvantage to have this kind of conjunctival bridge. It was a difficult matter to deal with post-operative prolapse in these cases, but in an uncomplicated case it was an advance on the usual procedure.

Mr. Bernard Cridland said that he had been carrying out this method for more than nine years and that when he first tried it, in order to give it a fair test, he adopted it in a series of consecutive cases without selection.

About forty-three cases were so dealt with, and in all but four a simple extraction was done. Some extractions proved rather difficult, more manipulation being required to express the lens than if no bridge had been cut. On the whole, however, the results were very satisfactory, especially as many of the patients operated on were "squeezers"—men accustomed to work in dusty trades, whose orbicular muscles were highly developed. When such a patient attempted to squeeze his lids together the wound did not gape, and there was no possibility of the upper lid engaging in the incision as might otherwise have happened.

A brief résumé of this series of cases had been given at a discussion held at the Oxford Ophthalmological Congress in 1922 on "Methods of Operation for Cataract."

The late Sir Anderson Critchett had opened the discussion and in his reply had emphasized the wisdom of being eclectic in operating for cataract, saying that no one fixed method was suitable for all cases. Since then he (the speaker) had been eclectic in his methods, and.

although he usually aimed at cutting a conjunctival bridge, he did not always do so. The value of the method lay in the more rapid healing of the incision and, as a consequence, a shorter stay in hospital, with more licence allowable to the patient in the days immediately following the operation.

For many years he had only thought it necessary to cover the operated eye and, when a bridge of conjunctiva had been left, there was all the more justification for this humane indulgence to the patient.

The question of the performance, or not, of an iridectomy rested entirely upon the type of incision that one was able to make. It was not always possible to ensure that an incision was entirely limbal, for occasionally the inner or outer part was a little corneal, and in these cases it was advisable to perform an iridectomy.

Mr. WILLIAMSON-NOBLE said that this operation was not difficult. He had been using an oblique bridge, cutting upwards and outwards. There had been prolapse in one or two cases, and he had passed an iris repositor under the bridge, and so freed the conjunctiva: he then placed curved iris forceps underneath and grasped the iris on the far side. A radial incision was made through this, after which it was a simple matter to drag the iris under the bridge and cut it on the other side. If this could not be done, the bridge could be cut through and the technique was then the same as if no bridge had been made.

Mr. M. S. MAYOU said that some years ago[1] he took cultures from various parts of the conjunctival sac. The upper fornix was nearly always sterile, while the lower fornix contained organisms, as also did the caruncle. He never turned up the upper lid to wash out, or swabbed the conjunctival sac; it disturbed the patient before the operation, and he did not think it necessary. Attention should be directed to the lower conjunctival sac. It might well be different in India, where the conjunctiva was, almost invariably, very dirty. As to opening the capsule before making the incision, that was creating unnecessary difficulties, as it made the eye soft. One could open the capsule with the point of a knife, in passing it across the anterior chamber.

Mr. A. B. NUTT said that there were two points he wished to mention. Mr. Pooley always made a bridge in his extractions, but it was not quite complete, being partially divided above and to the outer side; thus making the delivery of the lens and the subsequent iridectomy very much easier. Mr. Pooley almost always performed a peripheral buttonhole iridectomy. It was quite small, but it prevented the tendency to prolapse. The results were always good. He (the speaker) had himself been following the same method, and had found the partial bridge helpful.

Mr. R. AFFLECK GREEVES said that the most important thing about the conjunctival flap was to take care to get a good fringe of conjunctiva all the way round the section, bridge or no bridge.

Mr. F. JULER said that he had seen the beautiful films of operations on the eye, which were shown in Amsterdam a year ago, but this film of Mr. Fleming's was even better than those. He (the speaker) had attempted once or twice to have a cinematographic picture made, hoping that it might be useful for teaching undergraduates, but the present film indicated that such a method was well adapted for teaching graduates as well.

Mr. R. LINDSAY REA said that in the picture of eye operations shown at Amsterdam he had been horrified to see the knife cut through the cornea with a single stroke. Mr. Fleming's picture finely illustrated the contrast between the methods pursued.

He (the speaker) had worked both with the bridge method and without, according to the depth of the eyeball in the socket. It was better to use a bridge of the conjunctiva if the eye was prominent, but not if the eye was sunk in the orbit. With regard to prolapse of the iris, operating with a dilated pupil and a drop of atropine in the conjunctival sac at the same time, prevented prolapse afterwards, and this was his (the speaker's) usual method.

Colonel KIRKPATRICK said that he had used this technique for some years. One of its great advantages was that by its means elderly people were much more safely treated; the operated eye could soon be released from the bandage, and the patients were able to resume their ordinary life at an early date.

O'Brien's method of inducing paresis of the orbicularis by injecting the facial nerve in the neighbourhood of the temporo-mandibular joint, with novocain and adrenalin, was most

[1] Jacksonian Prize Essay, 1904.

helpful, since by this means a better exposure of the upper fornix was obtainable and the fashioning of a good conjunctival bridge was facilitated.

Mr. MALCOLM HEPBURN said he did not think that any kind of section—whether it was a corneal section, a conjunctival bridge or any other modification—would make any difference in regard to prolapse of the iris, which depended on the condition of the iris itself. Often when the section had been made, the iris appeared to be flabby and did not act briskly after evacuation of the anterior chamber. One could thus judge whether it would be likely to prolapse or not and therefore whether one should perform a simple or a combined extraction. Until the section was finished the operator could not decide as to the condition of the iris which was merely masked by the putting in of atropine.

Sir RICHARD CRUISE said that the most important step in the prevention of prolapse was to saturate the patient with atropine beforehand, so as to contract the iris into a rigid peripheral ring. In his own private operations he had not had to perform iridectomy because of prolapse during the last fifteen years, and he never did anything but simple extraction. He had never had a case in which the iris was prolapsed right out, requiring iridectomy; that was because, with the patient under atropine and the iris contracted into a peripheral ring, it was easier for the aqueous to escape over the rim, from the posterior chamber, than to push a comparatively rigid ring of iris tissue before it into the incision. The ideal iris dilated so fully as to give almost an appearance of an iridia.

Mr. NORMAN FLEMING, in reply, said that with regard to iridectomy, no hard-and-fast rule could be laid down to the effect that it should never be performed. There were circumstances in which iridectomy was a wise procedure.

In reply to Mr. Mayou he (the speaker) did not evert the upper lid, as he considered it was unnecessary to do so. At Westminster Ophthalmic Hospital it was the routine practice to evert the upper lid in washing out the eye, and in doing so it was practically impossible to avoid touching the palpebral conjunctiva with the finger.

Cataract from exposure to X-rays.—R. FOSTER MOORE, F.R.C.S.

The patient, W. T. S., a man aged 28, was first seen by Dr. A. C. Roxburgh and Dr. Dudley Stone on December 16, 1926 on account of severe sycosis of the scalp, face and neck, from which he had at that time suffered for three years, during which time he had been to a number of hospitals for treatment; the treatment had included X-ray therapy, but this, he stated, had made him worse.

Dr. Roxburgh and Dr. Stone agreed in believing that the only possible chance of cure was by a thorough irradiation of the whole face and neck and that this entailed certain risks. In view of these risks and the possibility of the patient changing his mind, Dr. Stone was unwilling to undertake treatment without first obtaining a signed statement from the patient that he was prepared to undergo it. He was willing to accept almost any risk if there was a prospect of cure, and it was afterwards learned that he had contemplated suicide on more than one occasion on account of the disease. Of the condition itself Dr. Stone says:—"The sycosis was as bad as ever I have seen it, covering the whole of his face and eyelashes, and in one or two places encroaching on his hairy scalp.

Irradiation was commenced on February 1, 1927, and the last treatment was on June 30 of that year.

The following are Dr. Stone's notes on the treatment:—

"X-rays through 1·0 mm. aluminium spark gap $13\frac{1}{2}$ in. Distance 58 cm. Dose given, 9 Holtzknecht units, or $1\frac{1}{2}$ Sabouraud.

"In this treatment I protected the nose and other parts not affected. Right and left side of face treated.

"February 14, 1927.—Complete epilation did not occur. There were some fixed hairs left in the cheek and neck.

"February, 24, 1927.—Softer rays were used, the spark gap being 6 in. and the filter just a piece of cardboard. The rays were directed from the forehead downwards across the face obliquely, and the right and left side of the face were treated at a distance of 28 cm., 5 Holtzknecht units given.

"In the frontal treatment the nose, upper lip and front part of the chin were protected, these being completely epilated before.

"March 14, 1927.—There was considerable improvement. A small area on the chin had broken out again.

"March 21, 1927.—The right and left side were again treated with the same filter and the same dose given.

"A third area with the rays centred on the chin and directed upwards was treated. This included the whole of the face and neck.

"June 30, 1927.—Dr. Roxburgh saw the patient on this date and further treatment was agreed upon. He also gave him an ointment to relieve the irritation.

"There were still signs of the disease in the eyebrows and eyelids, right side of face and a small area behind the right ear. All these areas were treated separately at the same distance and filter as the last two. This was the last X-ray treatment.

"August 24, 1927.—The patient reported that he had all his teeth out since the last treatment, at my suggestion, and the notes say that there were a few minute remaining hairs on the left upper lip and right temporal region.

"January 30, 1928.—There was no obvious focus left. The eyelids were red and inflamed, but no hairs were anywhere to be seen on the face."

The total dosage amounts to very nearly 12 Sabouraud doses in a period of five months, all centred in the face and neck.

It can be stated that this treatment completely cured the sycosis. There has been no trace of recurrence of the disease itself, and it is more than three and half years since treatment was completed. Telangiectases gradually appeared. These were well marked on October 3, 1929 (fig. 1), and have remained apparently unchanged to the present time.

About November, 1929, the patient's sight began to fail. The onset was gradual so that he is not able to date it accurately, but on March 19, 1929, the acuity was $\frac{6}{12}$ in each eye. He could read a paper quite well and believes that in October, 1929, he could see as well as ever he had done in his life, but since Christmas of that year he has been unable to read a book.

I saw him in June, 1930, when his visual acuity was $\frac{6}{60}$ in each eye, and he had a plaque-like opacity in the posterior cortex of each lens (see Plate). The opacity was not limited to this plaque for extending outwards beyond its limits was a finer powdery sort of opacity which gradually faded out towards the periphery. This is not sufficiently indicated in the figure. The fundi were normal.

On May 10 I needled the right cataract, and on October 12 Mr. J. G. Milner needled the left one for me. The process of absorption was uneventful, and after capsulotomy the acuity of the right was $\frac{6}{6}$. The absorption of the left lens is not yet complete but is running a normal course.

It may be noted that after removal of the lens substance, the original pattern of the lens opacity was still visible on the posterior capsule. There can be no doubt, however, that the greater part of the opacity was in the lens substance, adjacent to the posterior capsule.

The first case of cataract resulting from exposure to X-rays was reported by Leslie Paton in 1909 (*Trans. Ophth. Soc. U.K.*, 1909, xxix, 37). His patient had had, in all, thirty-eight exposures for lupus of the cheeks. Apparently, nine months after the completion of treatment her sight began to fail, and two years later she was able to count fingers only. The main opacity in the lens is described as a "greyish-white granular plaque probably lying against the posterior-capsule." The fundi were normal and the acuity was $\frac{6}{6}$ after removal of the cataract.

More recently two other cases have been reported by Jess (*Abst. Annales d'Oculistique*, 1929, clxvi, 165), in one of which the X-ray treatment was for a pituitary tumour and in one for a nasopharyngeal tumour. It is of interest to note that in these cases too, the opacity is described as being in the posterior cortex of the lens, and that it came on three and a half years after the treatment.

Showing the opacity in the posterior cortex of the lens.

It will be observed that in all these cases the dosage has been heavy, and efficient protection of the eyes has not been possible. It would seem that in spite of such exposures the only part of the eye to suffer has been the lens.

It strikes one as remarkable that the development of the opacity in the lens has been so long delayed, and whilst it is not possible to state with accuracy the dates of the commencement of the change, in the present case there was no defect of sight noticed by the patient until about two and a half years after the last irradiation, and the three other cases quoted are not very dissimilar to this.

It would be interesting to hear to what extent delayed results of X-ray exposures have been demonstrated, or are recognized as occurring in other tissues of the body.

FIG. 1.—Showing well-marked telangiectases.

I suppose it would be possible to protect the eyes efficiently when irradiation of immediately adjoining parts is required, and when, as in the present instance, the eyelids need treatment, I imagine that a properly shaped metallic shield could be contrived to be placed in contact with the eyeball within the conjunctival sac.

Discussion.—The PRESIDENT said that radiologists ought to know of this case; some means of protecting the eye should be devised.

Mr. M. S. MAYOU said that some years ago he had shown a case which had been treated with X-rays for exophthalmic goitre, and in which cataract had developed. There were telangiectases all over the exposed area. The eyes had not been specially protected

during the treatment. The cataract was mature, and he did not remember whether there were definite spots on the capsule such as were present in Mr. Foster Moore's case.

Numbers of X-ray operators had been exposed to the rays in the early days when no protection was used. Some of these had telangiectases of the conjunctiva, and some showed lens changes. Probably massive doses of the X-rays, rather than continued exposure of a moderate degree, were responsible for the production of cataract, by causing death of the epithelial cells lining the anterior capsule.

Mr. TREACHER COLLINS said that two years ago, at a meeting of the Ophthalmological Society, the late Dr. Critchley allowed the speaker to show him to the members. Dr. Critchley had been using X-rays for some years at the Metropolitan Asylums Board Ringworm school, and a peculiar patch of xerosis had developed on the ocular conjunctiva of his right eye. He also had, in each eye, a posterior polar cataract. A drawing of the conjunctival condition would be found in the "Transactions" of that Society. Dr. Erggelet, a German ophthalmic surgeon, was present at the meeting and drew his (Mr. Treacher Collins') attention to an article he had published in the *Zeitschrift für Augenheilkunde*, 1928, describing several cases of cataract after exposure to X-rays, in men who used the rays in the course of their employment.

Mr. NORMAN FLEMING suggested that in cases in which the eyelid had to be exposed to the rays, contact-glasses made of lead-glass should be put in during the treatment.

Mr. LESLIE PATON said that the cataract in his own case, shown in 1909, had not been absolutely on the posterior capsule, but was somewhat like the so-called "Coppock cataract," which the late Mr. Doyne had described. There was a biscuit-shaped cataract near the posterior pole, but he did not think it was actually in contact with the posterior capsule.

In his (the speaker's) case the patient had retained excellent sight for many years and then had retinal detachment in one eye. In the other eye, in the hope of getting a section of the lens, he tried to perform a Smith's operation, with the result that there was considerable prolapse of the vitreous, and the sight in that eye was never quite so good. For many years the patient had $\frac{6}{4}$-vision in the eye first operated on. Subsequently, however, she had detachment in both eyes. He did not know whether that was due to injury to the vitreous at the time of X-ray exposure.

Mr. Cridland had concluded that in iron puddler's cataract the opacity was very near the posterior pole.

Mr. FOSTER MOORE (in reply) said that the opacity, in the Coppock cataract, was behind the nucleus but well clear of the posterior capsule, whereas in this case there was no doubt that it was in contact with the capsule, for when the lens substance was completely absorbed, there was the exact pattern of what was seen on the screen impressed, so to speak, on the posterior capsule which remained.

Mr. Leslie Paton showed an instrument for demonstrating to a few students the forms of diplopia resulting from paresis of various muscles.

Section of Surgery.

[*January 7, 1931, continued.*]

A Series of Urograms of Cases illustrating the Uroselectan Method of Intravenous Pyelography.—JOHN EVERIDGE, F.R.C.S.

I do not consider that intravenous pyelography has ousted the older (retrograde) method, but the series of urograms now shown illustrate the special type of case in which intravenous pyelography (by the uroselectan method) is especially indicated. Such cases may be classified into the following groups:—

(I) Children, especially male children.
(II) Nervous intolerant adults.

FIG. 1.—Shadow of a stone in the lowest calyx of the left kidney in a boy aged 8 years.

(III) Cases to demonstrate the condition of the kidney when ureter catheterization was impossible, owing to ureteric obstruction.

(IV) Cases to demonstrate the value and importance of "contrast pyelograms": (*a*) In renal hæmaturia, e.g., to demonstrate a filling defect due to a tumour, etc. (*b*) Renal pain: several examples of hydronephrosis were shown. (*c*) Renal tuberculosis.

(1) *Localization of renal calculi in a child.*—A case of localization of a calculus in the kidney in a boy aged 8 years. The stone is lodged in the lower calyx (fig. 1)

FIG. 2.—A stone shadow which lay well in front of the vertebræ. Without pyelography it might have been mistaken for a gall-stone, etc.

(2) *Localization of renal calculus in an adult.*—A case of stone in the kidney in a very intolerant female, who would not submit to instrumental pyelography. It might be thought from the photograph that the shadow is a gland, or perhaps a gall-stone; it is well in front of the anterior margin of the vertebræ (fig. 2). A uroselectan pyelogram shows the shadow in the position of the lowest calyx of the kidney (fig. 3). It was a stone, and was removed by operation.

(3) *Where ureter obstruction prevents the passage of a catheter.*—In a patient who complained of pain in the kidney region, it was absolutely impossible on cystoscopy to discover the orifice of the ureter on the right—the painful—side, even after indigo-carmine injection. Uroselectan pyelography showed an enormous dilatation of the kidney and ureter (fig. 4).

FIG. 3.—The shadow observed in figure 2. It was a stone situated in the lowest calyx of the right kidney.

Fig. 5 shows shadows in the kidney region, and also a shadow in the lower end of the left ureter, caused by a stone which prevented the passage of a catheter. The question in this case was whether the upper shadows were due to glands, or to stones in the kidney; the pyelogram shows the shadows to be in the pelvis of the kidney (fig. 6). They were stones.

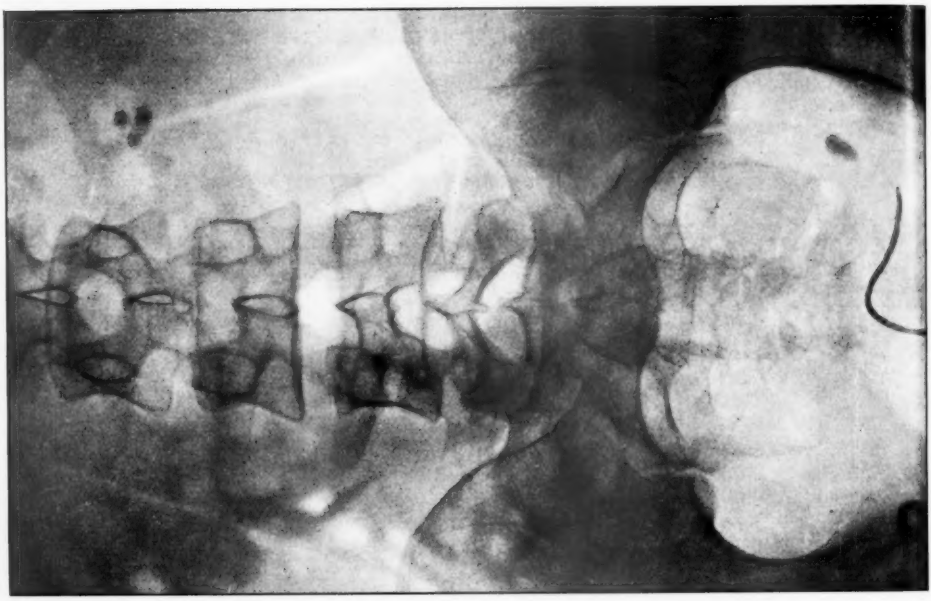

FIG. 3.—Doubtful shadows in the left renal area. A calculus lodged in

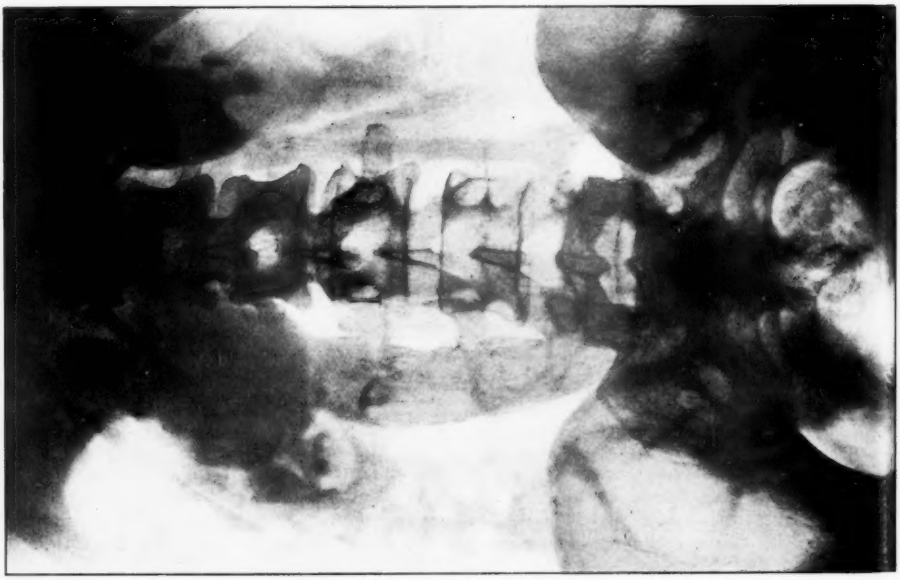

FIG. 4.—Hydronephrosis and hydroureter in a case where the

FIG. 4.—Hydronephrosis and hydro-ureter in a case where the

FIG. 5.—Doubtful shadows in the left renal area. A calculus lodged in

FIG. 6.—The shadows in the renal region of figure 5 lay within the area of the dilated pelvis.

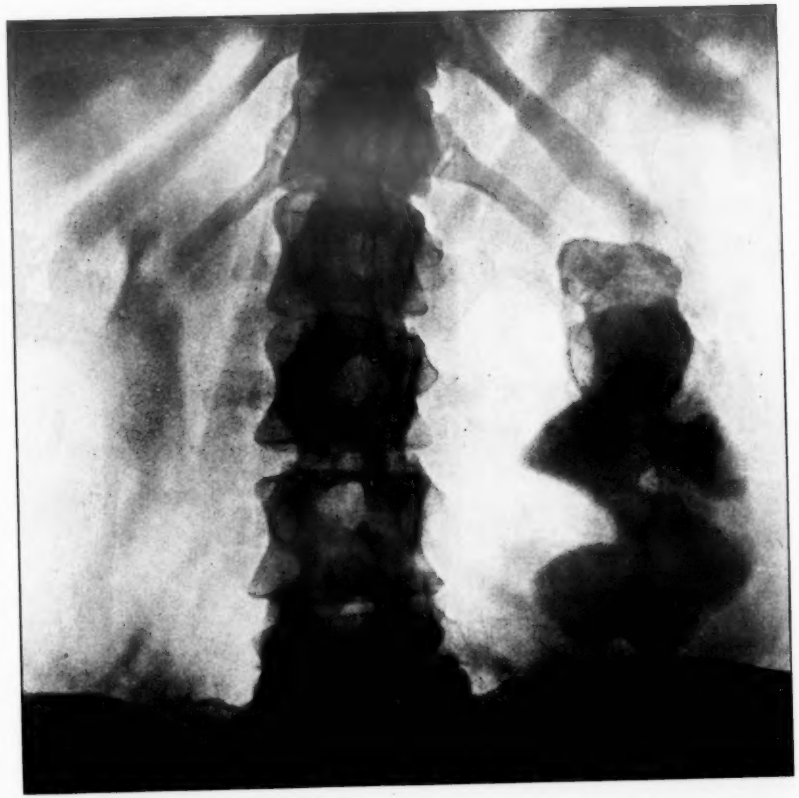

FIG. 7.—Huge left kidney calculus. Intravenous pyelography was used as a means of ascertaining the condition of the right kidney since its ureter could not be catheterized. It (the right) is an obviously defective kidney.

In the next case a skiagram showed an enormous stone in the kidney, and the question arose as to whether it was justifiable to remove that kidney, i.e., whether the other kidney was adequate for carrying on the function. It was not possible to pass a catheter up the ureter on the opposite side, and indigo-carmine did not escape from the opposite ureter, therefore it was difficult to know how to proceed in this case. I took a series of intravenous pyelograms, and what I now show is the best shadow I could get (fig. 7), and I assumed, from the fact that there was no escape of urine, that it was unsafe to operate on that patient.

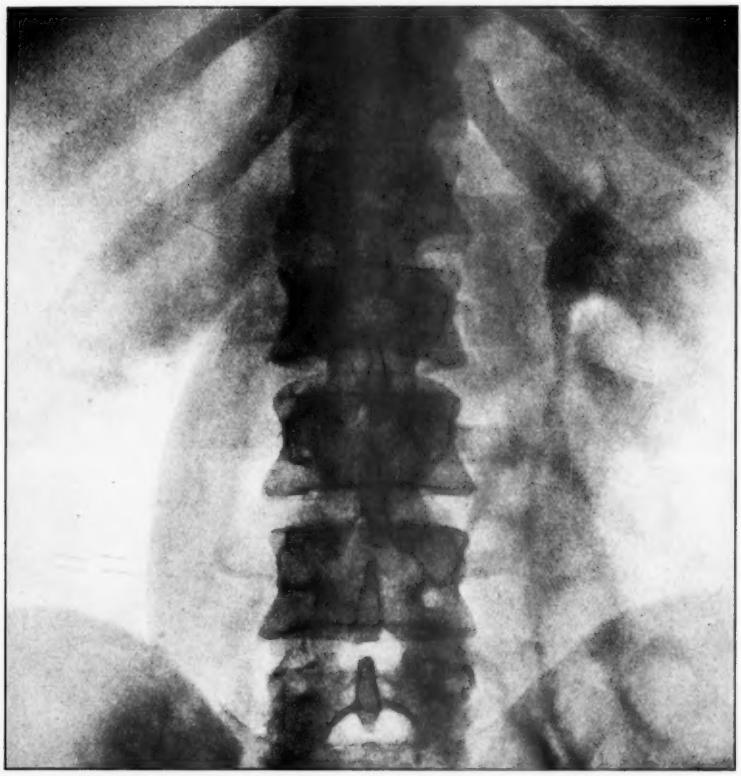

FIG. 8.—Filling defect of the right kidney due to a hypernephroma. This photograph revealed the source in a case of painless hæmaturia where cystoscopy was negative.

(4) *Contrast pyelograms* : (*a*) Renal hæmaturia.—In the next case, that of a man, aged 50, a thick, muscular person, it was not possible to examine the abdomen; it was too rigid. The patient had had three attacks of hæmaturia. Cystoscopy showed nothing abnormal, therefore I decided to have a uroselectan pyelograph made. The left urogram is normal, and there is an indefinite shadow on the other side; this is a very inefficiently filled pelvis of the right kidney (fig. 8). The value of this pyelogram was that it at once gave us an idea upon what to work. The condition at operation was found to be due to a very large growth of the kidney.

(*b*) Renal pain.—(i) An apparently healthy man, aged 32, had pain in the right kidney region. By uroselectan pyelography two enormous hydronephroses were shown. The best shadows appeared two hours after the injection (fig. 9). All the pain was in the right kidney region, yet the left kidney was even more affected than was the right. The renal function tests were low, and the urea concentration was under 1·5. I cannot explain the cause of this condition; there was no obstruction in either ureter, so far as the passage of a catheter showed. (ii) A young female patient had pain in the left kidney region. Uroselectan pyelography was carried out, and the right side showed up well. Nothing appeared on the left side (fig. 10), therefore a retrograde pyelography was done, by the catheterization method (fig. 11).

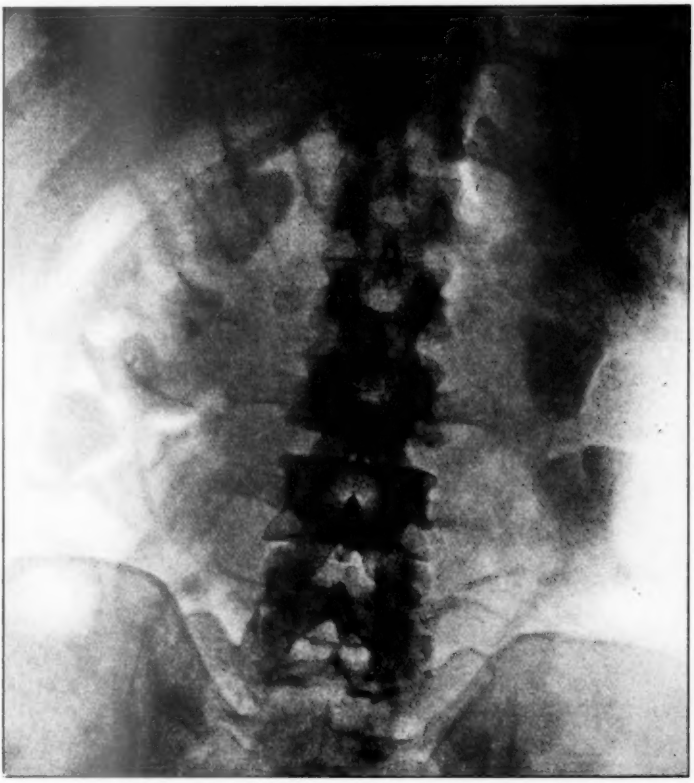

FIG. 9.—Huge bilateral hydronephroses. Pain was only experienced in the right kidney.

Subsequent operation revealed a most unusual kidney [shown], small and atrophic, with hydronephrosis, and an obstruction at the upper end of the ureter.

(*c*) Renal tuberculosis.—So far, we have no standard pyelogram for renal tuberculosis; all we can say at present is, that when there is advanced tuberculosis of one kidney we can never get, in a series, a normal pyelogram within the first two and a half hours after injection. There is a definite dilatation of the ureter (fig. 12).

I think that in these types of cases intravenous pyelography is of very great value, and introduces a new step in the investigation of urinary cases which will be, I feel sure, epoch-making.

FIG. 10.—A case of left renal pain. No urogram is visible on the left side, and figure 11 explains its absence.

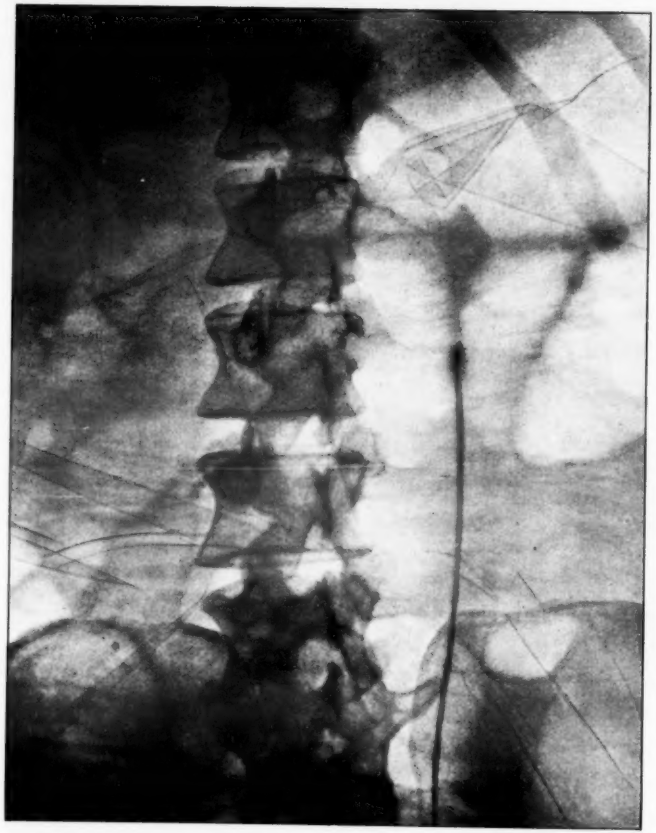

FIG 11.—Instrumental pyelography of the left kidney in the same case as figure 10. Nephrectomy revealed an atrophic kidney and a valvular stricture at the uretero-pelvic junction.

FIG. 12.—Right renal tuberculosis. Note dilated (ulcero-cavernous) calyces, and the patented ureter.

I owe a debt of gratitude to Dr. Graham Hodgson for his collaboration and for the loan of his negatives.

Discussion.—Mr. KENNETH HERITAGE said that he was particularly interested in the relative atoxicity of uroselectan when administered intravenously. He had recently seen this drug administered for diagnostic purposes in a case of gross pyuria in which the retrograde method was impossible, owing to the severe purulent cystitis. The condition proved to be one of bilateral pyonephrosis with a blood-urea of 140 mgm. Far from causing the patient inconvenience, the drug seemed to have a beneficial effect. The findings were in keeping with the other evidence of renal insufficiency, and sufficed to indicate the better of the two sides, and a pyelostomy was performed. The only cases of death after intravenous urography with which he was acquainted, viz., those of von Lichtenberg, were, he understood, due to the progress of the disease and in no way attributable to uroselectan. He was able to confirm Mr. Everidge's observation on the dilated appearance of the ureters common in tuberculous cases. He (the speaker) suggested that this appearance, apart from being caused by a tuberculous stricture in advanced cases, might be due to ureteral fibrosis interfering with the normal peristalsis. This ureteric "hold up" rendered cases of renal tuberculosis some of the most successful subjects of intravenous urography, apart from the undesirability of subjecting such cases to prolonged retrograde catheterization.

With increased attention devoted to radiological examination of the upper urinary tract, the condition of pyelectasis, or idiopathic dilatation of the renal pelvis, in the absence of any obstructing factor, was being discovered with increased frequency. It would appear that there was a lack of dynamic continuity between the pelvis and ureter, which did not give rise to symptoms unless infection were superadded. [An abrodil urogram of such a case was shown.] It was satisfactory to note that in all Mr. Everidge's cases in which a kidney had failed to excrete the drug, subsequent investigation had yielded ample explanation of that kidney's lack of function, by showing gross destructive disease. In other words—"no shadow, no function," could be accepted, keeping in mind, however, the several observations on record of failure of excretion of the drug on one side when given shortly after attempts at retrograde pyelography on that side. For this reason intravenous urography should precede instrumentation.

Since November, 1930, he (the speaker) had employed abrodil (sodium non-iodo-methane sulphonate) for intravenous urography, in preference to uroselectan. Its high iodine content, 52%, allowed of the employment of a smaller dose, at the same time obtaining good radiological definition. Also its high solubility and low toxicity rendered its administration in the majority of cases free from any sensory disturbance whatsoever. Time also was saved, since in a normal case the pelvis showed within five minutes, and reached a maximum density in fifteen to twenty-five minutes. Probably the three most important points in obtaining good excretion pictures were: Restriction of fluids for from twelve to sixteen hours before the examination. Fairly rapid and neat injection of the solution, and abdominal compression by the Potter-Bucky belt during the exposure.

Mr. EVERIDGE (in reply) said that he had not used the method in cases with low renal function; he had been afraid to do so. Only one death was on record following its use; that had occurred in Berlin, and was in a case in which the kidneys were functioning badly. It implied the warning that the method must not be used when the kidneys were not functioning. He had had only one case in which there was a somewhat low renal function, but the patient was young (32 years) and otherwise in very fair health. The youngest patient in whose case he had carried out the investigation was a boy aged 8, and the case was included in the series shown.

Microscopical Appearances of Interstitially Radiated Tissues.

By SIR LENTHAL CHEATLE, K.C.B., F.R.C.S.

I HAVE to thank Dr. J. A. Murray for allowing these investigations to be made at the Laboratories of the Imperial Cancer Research Fund, and I am deeply indebted to Dr. R. J. Ludford, who carried out, with great care and trouble, the preparation of the specimens from which these photographs were taken.

The action of interstitial radiation upon carcinoma includes:—

(*A*) The direct action on the carcinoma cells.

(*B*) An indirect action upon the tissues of the host.

(*A*) The direct action upon the carcinoma cells depends upon the intensity of the radiation and the character of the cells. Intense radiation induces an effect comparable to cauterization. With less radiation the cells may be altered without being killed; the nuclei and cytoplasm undergo enlargement followed by degeneration (fig. 1), and various irregularities of mitosis also occur. Similar abnormal mitoses are also found in radiated normal epidermis (fig. 2). More rapidly growing cells are as a rule more susceptible to radiation than those that are growing more slowly, hence the greater susceptibility to radiation of carcinoma cells compared with normal cells (fig. 3).

(*B*) It is doubtful how far direct action upon the carcinoma cells can explain all the clinical results of regression of a tumour. It is possible that the reaction of the tissues of the host may be of considerable importance in inducing effects inimical to the tumour cells. These reactions of the host include an action on the stroma

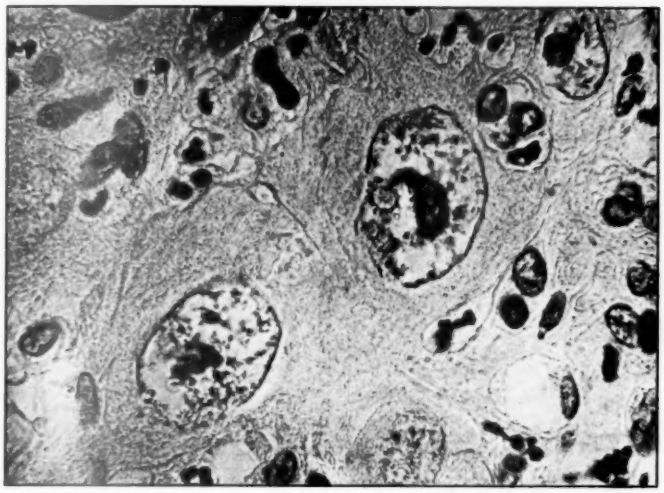

FIG. 1.—Two enlarged carcinoma cells from part removed immediately after seven days' interstitial radiation (element) : carcinoma of lip.

FIG. 2.—A basal cell in a state of abnormal mitosis from the normal epidermis removed immediately after seven days' interstitial radiation (element).

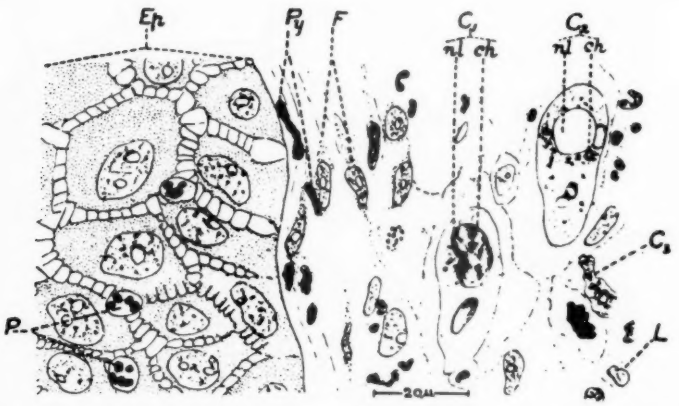

FIG. 3.—Drawing of parts removed from a squamous epithelioma of lip immediately after seven days' interstitial radiation. (Ludford.)

Ep, apparently unaltered normal epidermis cells from another part of which the abnormal mitosis in fig. 2 was discovered. *P*, polynuclear leucocytes. *Py*, pyknotic nucleus of a damaged fibroblast. *F*, fibroblasts. *C1*, enlarged carcinoma cell in a state of degeneration. *nl*, nucleolus. *ch*, chromosomes. *C2*, enlarged carcinoma cell in a later state of degeneration. *C3*, a dead carcinoma cell. *L*, dead leucocytes.

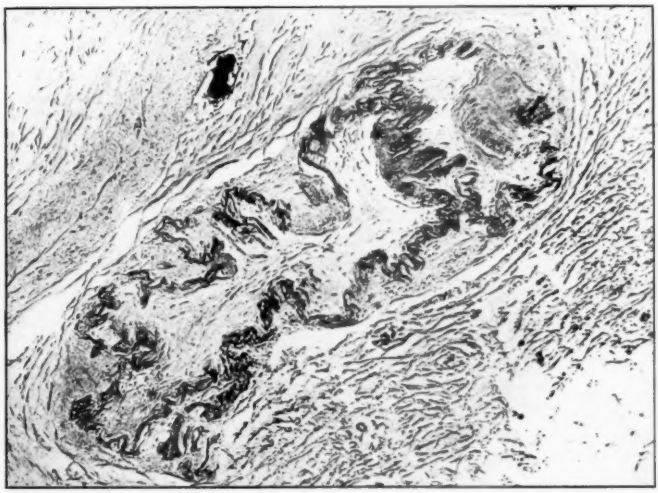

FIG. 4.—An organized thrombus in a vein six months after interstitial radiation of a breast (element).

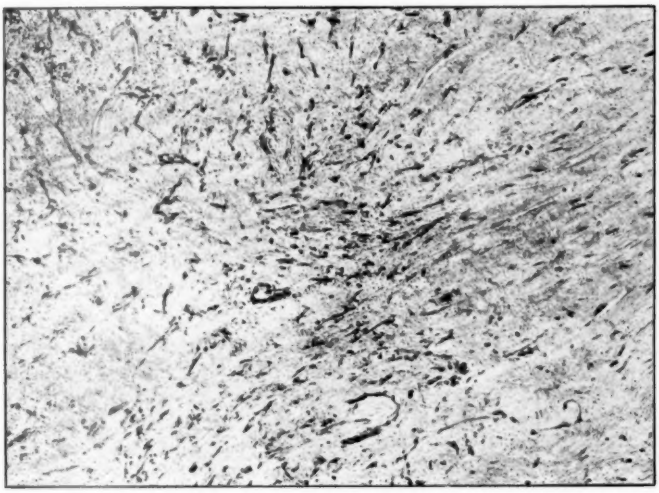

FIG. 5.—Cicatricial tissues amongst which are dead carcinoma cells, six months after interstitial radiation of a breast (element).

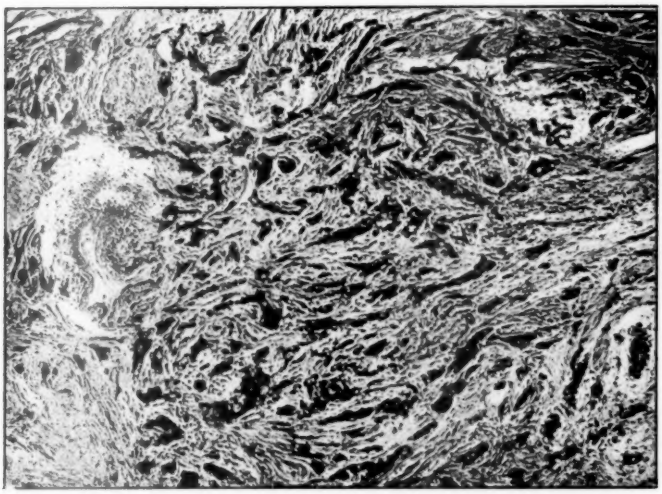

FIG. 6.—Area of apparently unaltered carcinoma cells from same case as fig. 5. An organized venous thrombus is seen on the left.

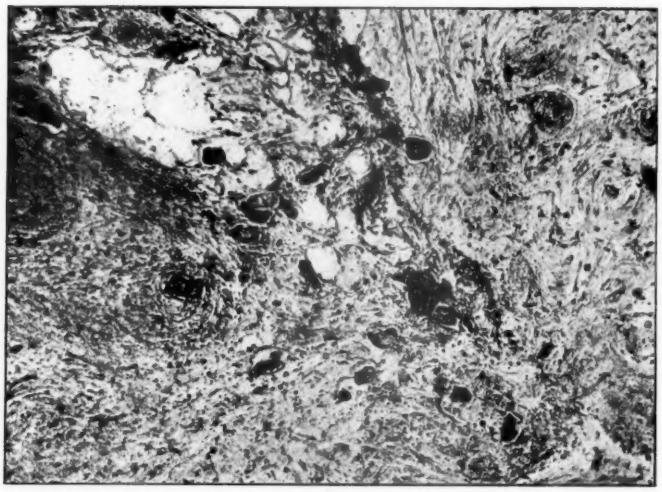

FIG. 7.—Groups of apparently unaltered carcinoma cells from the margin of another interstitially radiated breast, six months after removal of the element. There are many dead carcinoma cells amongst the cicatricial tissue seen in this photograph.

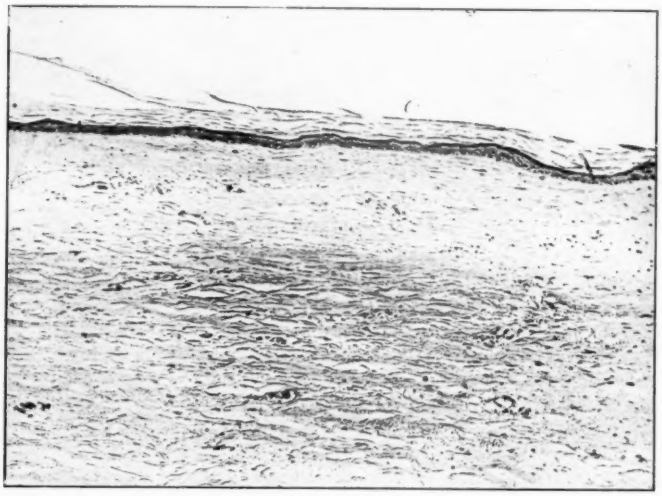

FIG. 8.—Skin overlying the interstitially radiated breast (element) of fig. 7.

including the blood-vessels. There may be hæmorrhage (W. Cramer) and thrombosis and eventually obliteration of the vessels by organization of the blood-clot, as well as other vascular changes (see fig. 4).

The formation of cicatricial tissue after radiation is a marked feature of the tissue reaction. The constriction of this cicatricial tissue may exert so great and continuous a pressure upon the carcinoma cells as to cause their atrophy (fig. 5).

So little is known about normal "trophic" conditions that it is not of practical value to discuss them, but they may also be profoundly changed by radiation.

In spite of apparently efficient interstitial radiation there too often remain carcinoma cells that look morphologically as viable and as vigorous as non-radiated carcinoma cells (see figs. 6 and 7). These particular cells, although they appear morphologically to be active carcinoma cells, may in fact have been so biologically altered that they are no longer dangerous. On the other hand they may be completely active carcinoma cells that have not been affected by radiation. Fig. 8 shows the effect of interstitial radiation upon the overlying skin six months after the application of the element. The papillary layer has disappeared and although there was no sloughing of the skin, it was as if the condition was one of a recently healed ulcer. The sebaceous glands have disappeared and all that can be seen of the hair follicles are the remains of the arrectores pilorum. The affected skin was dry, desquamating and of a dull red colour.

Sarcoma of the Kidney in an Infant.—CECIL P. G. WAKELEY, F.R.C.S.

The specimen was removed from a female infant aged one year and ten months, and shows half of the tumour removed at operation. The tissue is homogeneous, and has a definite capsule. Only a slight amount of renal tissue is present, at the lower part of the specimen.

Microscopic examination of the tumour shows a homogeneous round-celled sarcoma, with a fairly vascular stroma. No renal tissue can be seen.

Clinical history.—Patient was admitted to hospital August 20, 1926, with a history of having passed a large amount of bright blood in the urine on August 17, with decreasing amounts on the two following days. This was the first symptom, and no pain whatever had been noticed.

On admission.—A swelling was visible and palpable in the right flank, and hypochondrium, extending downwards for three inches and a half from the costal margin, and to within one inch of the middle line. It was smooth, round, and hard; was not tender; moved with respiration.

The urine, on examination, showed pus cells, red blood-corpuscles, and mucus. The blood-urea and urea concentration tests were normal. Nephrectomy was performed, August 30, 1926, through a vertical incision three and a half inches long, splitting the right rectus.

Recovery was uneventful; the patient was seen at six-monthly intervals after the operation, and showed no signs of any secondary deposits. However, the patient died in December, 1927, after measles, and no autopsy was obtained.

Discussion.—MR. JULIAN TAYLOR asked whether Mr. Wakeley had satisfied himself that the disease from which the child had died was really measles. In many cases of malignant disease of the kidney, children died with pyrexia when they had recurrence.

Mr. EVERIDGE asked if the child had a rise of temperature before the operation, and by what method Mr. Wakeley had performed the nephrectomy. He (the speaker) had brought to the meeting a kidney which he had removed from a child aged 18 months; it was very large. Before the operation the child had a temperature of 103° to 104° F., and within three days after the nephrectomy—which the child stood very well—the temperature was down to normal, and remained there during convalescence. Then he performed a lateral nephrectomy, making an incision straight down the flank in the anterior axillary line, and removed the kidney by the extra-peritoneal route.

Mr. WAKELEY (in reply) said that the home of the patient was fifty miles from London, and the report of death from measles came from the general practitioner. The child had no increased temperature before—or at the time of—operation. He had employed the abdominal route; the tumour was a large one, and it would have been impossible to get it away through a lumbar incision. In children he used the abdominal route because it enabled an examination to be made of the other kidney, to see if there were any secondary deposits. On two occasions he had, in that way, found secondary deposits under the diaphragm.

CASES SHOWN BY A. J. GARDHAM, M.S.

(1) Teratoma in the Cheek of a Child, aged 3 weeks, producing a Teratomatous Metastasis in bone at the age of 16 months.—A. R., admitted to hospital, 1928, when 3 weeks old, with the history that a lump had been noticed inside the left cheek at the age of 9 days. The tumour had increased from the size of a pin's head to that of a halfpenny.

Operation, 15.6.28.—Enucleation of tumour from inside mouth. Re-admission one month later, with local recurrence.

Operation, 30.7.28.—Cheek split and recurrent tumour removed. There was a pedicle extending backwards internal to the ramus of the jaw into the substance of the internal pterygoid. Discharged, healed, 14.8.28.

Re-admitted fourteen months later, with history of swelling of right arm for one month. Right humerus expanded by central tumour. No evidence of growth in other bones.

Operation, 5.10.29.—Biopsy and insertion of 22 by 1 mgm. radium needles into tumour.

Subsequent Course.—Needles removed ten days afterwards. No immediate change in tumour.

Child since seen at intervals of a few months. Remains in good health and the condition of the arm is unchanged, except that in July, 1930, following a history of recent pain, a fracture was discovered. Successive skiagrams demonstrate slow increase in calcification and progress of normal growth proximal to tumour.

Microscopical examination. (1) Original tumour.—Teratoma showing cysts, lined with stratified or mucus-secreting epithelium; muscle, bone and cartilage and young connective tissue. (2) Second tumour in humerus.—Epithelium-lined cysts; mesoblastic tissue, consisting of spindle-shaped cells of irregular arrangement, containing blood spaces.

The case is interesting in that the recurrent tumour contains both epiblastic and mesoblastic tissue, showing malignant characters. I am not aware that such an occurrence has been previously recorded.

(2) Radium Necrosis of the Trachea following Insertion of Radon Seeds into a Carcinoma of the Thoracic Part of the Œsophagus.—H. B., male, aged 59. Admitted to hospital, 1929, with increasing dysphagia, of one month's duration. By X-ray examination and œsophagoscopy the presence of a carcinoma of the œsophagus at the level of the bifurcation of the trachea was established.

Operation, 31.1.29.—Extra-pleural exposure of œsophagus and insertion of ten radon seeds of one millicurie strength into the growth and the œsophagus above and below. Seeds were screened with ·25 mm. platinum only. Thorax closed without drainage.

Post-operative course.—Temperature varied between 99° and 101° for three weeks, after which an effusion in the right pleura was aspirated and the temperature fell to normal. Swallowing improved, and in the sixth and seventh weeks the patient was able to swallow a duodenal tube. Additional irradiation was then given by means of a fully screened 50 mgm. tube of radium enclosed within the duodenal tube. Discharged eighth week after operation.

Subsequent course.—Patient lived until August, 1929 (seven months), without a gastrostomy, swallowing soft solids without difficulty. On August 22 he was taken suddenly ill with broncho-pneumonia and died in an infirmary within a few days.

Post-mortem examination.—Lungs: bilateral broncho-pneumonia.

Œsophagus: Just above the tracheal bifurcation the œsophagus is narrowed to about half its diameter. On opening it a flat ulcer is seen in this position, about three inches by half an inch, with hard, very slightly raised edges. The ulcer has perforated the œsophageal wall and there is a small cavity between the œsophagus and trachea, in which lies a slough containing the remains of a tracheal cartilage.

Trachea: injected throughout. Just above the bifurcation is a circular punched-out ulcer, a quarter of an inch in diameter, showing a necrosed cartilage in its base. This ulcer has the characteristics of a radium necrosis. No secondary growths were present.

Microscopical examination (longitudinal edge of ulcer).—There is a considerable amount of actively growing carcinoma, but in some places the cells show the influence of the previous irradiation, being shrunken and separated from one another. The few vessels present show a fairly well-marked endarthritis.

(3) **Early Paget's Disease of the Nipple, with an Extensive Carcinoma of the Breast.**—E. S., aged 50. Admitted 12.11.30 complaining of a watery discharge from the left nipple for six months. The left nipple had almost completely disappeared. In its place was an ulcer, about one-six of an inch in diameter, covered with a crust. No definite mass was felt in the breast, but the whole of the upper and outer quadrant was indurated and attached to the deep fascia.

Operation, 17.11.30.—Radical removal of breast, pectorals and axillary contents. The glands below the clavicle showed growth macroscopically.

The specimen shows ulcerated nipple and growth remote from it.

Microscopical examination.—Breast: Carcinoma, mainly spheroidal-celled. The section includes a much dilated duct, with well-marked overgrowth of the epithelium, which appears at one place to be invading the surrounding breast tissue. Gland: Spheroidal-celled carcinoma. Nipple: Typical changes of Paget's disease in the deeper layers of the epithelium in several places. Epithelial overgrowth in the deeper ducts.

Tuberculoma of Occipital Lobe following Gunshot Wound of Head.—A DICKSON WRIGHT, M.S., F.R.C.S.

A. J., aged 33, in 1915 when in the Naval Division at Gallipoli, was wounded in the head and was unconscious for eighteen days. The bullet seemed to have traversed the occipital region with a wound of entry on the left and exit on the right. On recovering consciousness the patient was totally blind and remained so for two years, after which time a certain amount of sight returned. For the thirteen years following 1915 the wound continued to discharge and fifteen separate operations were performed during this time, for removing foreign bodies and sequestra, opening abscesses, inserting and removing celluloid plates, etc. In 1928, shortly after the wound healed, headaches became troublesome and increased in severity till eventually a severe headache was followed by an epileptic fit on November 20, 1929; a second fit occurred on February 10 and a third on February 15. Admitted to hospital on February 22, 1930. A stereo-skiagram taken at this time showed two large deficiencies in the skull and five spherical shadows in the right occipital lobe. The visual field showed a homonymous hemianopia to the right with no central vision in either eye. On March 3, 1930, five separate tumours, varying in size from that of a walnut to that of a pea, were removed from the occipital lobe by careful dissection with cotton wool. One of the tumours

was in the wall of the lateral ventricle. A wide opening was left in the ventricle at the completion of the operation. The pathologist reported these tumours to be chronic thick-walled abscesses containing caseous pus from which the *Micrococcus tetragenus* was obtained in pure culture. The convalescence was fairly stormy, a good deal of cerebrospinal fluid leaked away, and there was much headache and high temperature. Eventually the patient recovered and was discharged a month after the operation without any headache and feeling better than at any time since 1915. After three months' good health the headaches returned with increased severity and the sight deteriorated. He was re-admitted to hospital on November 11, 1930, and was operated on again four days later. The occipital lobe on the right side was exposed again after traversing the most dense scar tissue. A hard tumour was discovered stuck down in the angle between the falx and the tentorium, and extending as far forward as the cerebral pedicles. It was separated carefully from the surrounding brain by cotton-wool dissection and from the falx and tentorium by dissection with the knife. The lateral ventricle was again opened and the biloculated tumour shown was removed. The contents were caseous and the walls ¼ in. thick. Following operation, there was some anxiety for four days on account of post-operative pneumonia and profuse cerebrospinal fluid loss. Afterwards the patient made a rapid recovery and was discharged well fourteen days after the operation. He has since stated that he has no headache, his sight is better, and he is feeling well in every way.

The pathologist's report was that this tumour was not a chronic abscess as before, but a fibro-caseous tuberculoma with bacilli in the giant cells. An examination of the patient's chest revealed a suspicious area at the left apex, but there were no bacilli in the sputum.

The special points of interest in this case are :—

(1) The large number of cranial operations (seventeen in all) successfully negotiated by the patient.

(2) The value of stereo-skiagrams in all head cases. This patient had been seen previously by a cerebral surgeon, who, without taking a skiagram, had told him that he could do nothing for him.

(3) The lateral ventricle was opened on both occasions in a septic field without serious result. In fact the leakage of cerebrospinal fluid did not last as long as it usually does when the drainage is from the sub-arachnoid space. One anticipated a fulminating meningitis in this case comparable to the flare-up which occurs after operations on old gunshot wounds involving bone. As a prophylactic measure, and probably a feeble one, large doses of urotropine in an alkaline medium were administered before and after operation.

(4) It illustrates the fact that even in the most unfavourable cases, hope of cure by operation should not be abandoned.

Tuberculous Empyema Necessitatis. Hæmothorax due to Bleeding from a Cavity.—CHARLES NEWMAN, M.D.

The patient, a girl aged 18, first suffered from cough and night sweats in June, 1930. A pleural effusion developed on the left side, which was tapped three times in St. Giles' Hospital. Air was also found in the chest as well as fluid. A subcutaneous abscess formed round the tapping punctures, and was aspirated. Tubercle bacilli were found in the pleural fluid, but not in the sputum. The girl discharged herself from hospital, and was lost sight of till the following October, when Dr. Harold Moody was called in and found that the effusion had become an empyema, which had burst spontaneously through the second left space. The opening discharged freely, but the heart remained on the right side and the left lung did not expand. The abscess over the left lower ribs was converted into an ulcer, with undermined edges, about 3 in. in diameter, in the base of which three

openings into the pleural cavity had formed. Patient was admitted to King's College Hospital. A skiagram showed the pneumothorax and the collapsed lung, with the cavity inside it. The patient died three days after admission, from a sudden large hæmothorax.

At post-mortem examination the left lung was found to be completely collapsed, as shown in the specimen. It was held up to the apex of the pleura by two dense pillars of adhesions. A small cavity was found opening into the pleura; into its inner side a bronchus opens, and at the top can be seen an open artery. The rest of the lung contains patches of acinous nodose phthisis, which were drying up and appeared to be healing. The pleura is completely covered with tuberculous tissue, and the cavity was full of blood-clot. The liver showed extreme fatty degeneration of the portal zones.

The specimen is of interest as showing: (1) an empyema necessitatis, and (2) a fatal hæmorrhage into the pleura from a vessel in a tuberculous cavity, an excessively rare occurrence.

CASES shown by G. GORDON-TAYLOR, M.S., F.R.C.S.

(1) Diffuse Fibrocystic Disease of Bone, associated with a Parathyroid Tumour.—L. W., female, aged 20, gave a history of six months' pain in left leg, thigh and buttock.

On February 2, 1929, she had a spontaneous fracture of the left femur. Skiagrams showed a localized area of cystic rarefaction in region of the fracture. A diagnosis of fibrocystic disease was made and the leg placed in a Thomas's knee-splint with Sinclair's screw extension.

4.2.29.—Blood-calcium, 15·9; phosphorus, 3·0.

4.7.29.—As there was no union of the fracture, and as there were considerable changes in all the bones of the left leg, it was amputated through the hip-joint. X-rays showed the absence of cystic changes in the rest of the skeleton, but their density was not controlled.

In October, 1929, my attention was drawn to a similar case of Dr. Donald Hunter,[1] therefore the patient was again examined by X-rays and widespread changes in the rest of the skeleton were found.

5.10.29.—Blood-calcium, 8·2; phosphorus, 2·8.

In December, 1929, there was a spontaneous fracture of the right femur, and the patient was re-admitted to hospital. Examination of the neck failed to reveal any abnormal swelling, but the trachea was slightly displaced to the left, the blood-calcium was 11·6, and the phosphorus 3·25.

On January 9, 1930, the neck was explored and a tumour found behind the upper pole of the right lobe of the thyroid. It appeared to be extra-capsular and measured 3·5 by 2·5 by 2·5 cm. It was removed. A slightly hypertrophic parathyroid measuring 0·8 by 0·5 cm. was found behind the lower pole of the left lobe of the thyroid and was also removed. On the day following operation there were signs of neuro-muscular irritability and the blood-calcium was 10·5. By the fourth day severe tetany had developed; this persisted for about a week and was controlled by repeated intravenous injections of 5 to 10 c.c. of 1% calcium lactate with 50 to 100 units of parathormone. The tetany gradually diminished until after about three weeks the hands could be used freely. Chvostek's sign remained positive for six months. Throughout the period of severe tetany, estimations of blood taken before, during, and after attacks, showed the calcium to be between 9·1 and 10·5 and phosphorus between 2·4 and 3·9.

The fracture of the right femur slowly united, all pains were completely relieved and the patient was discharged from hospital during October, 1930, taking about

[1] *Proc. Roy. Soc. Med.*, 1929, xxiii, 227 (Sect. Med. 27).

30 gr. of calcium lactate daily by mouth. The blood figures are normal. She is still wearing a caliper and is therefore unable to walk, but there are signs that calcium is very slowly being redeposited in the bones.

(2) **Cystic Osteoclastoma of the Os Innominatum Successfully Treated by Inter-Ilio-Abdominal Amputation.**—W. J., male, aged 18, in December, 1928, whilst playing football, received a kick in the left groin, but was able to finish the game. Later had some pain in that region and, after treatment by a bone setter, attended the Middlesex Hospital. Examination then showed a firm indefinite swelling in the neighbourhood of the left pubic spine, also palpable in the perineum and by the rectum. There was slight limitation of all movements of the hip and slight wasting of the quadriceps.

Skiagrams (March 12, 1929) showed the shadow of a tumour involving the pubic and ischial bones and encroaching on the acetabulum, and on April 3, a repeat skiagram showed the tumour to have increased in size.

A tentative diagnosis of an ossifying sarcoma was made and an inter-ilio-abdominal amputation, with a single large posterior flap, was performed. Convalescence was uninterrupted and the patient was discharged on the forty-ninth day after operation.

A special webbing support, taking the weight from the right shoulder, was designed and is worn day and night. There is now no sign of stretching of the abdominal parietes. He sits comfortably and gets about with crutches, and will not consider a prosthesis.

(3) **Advanced Carcinoma of Rectum Involving Uterus and Vagina.**—Patient, female, 52 years old. Nine to ten months before admission to hospital she had complained of pain on defæcation and bleeding by the bowel. There was a history of constipation, which had become increasingly severe as time went on. Examination showed a large growth, from one to three inches from the anus, situated mainly on the anterior wall, through which a fistula was felt into the vagina.

Laparotomy was performed in February, 1930, and extensive infiltration by growth and inflammatory tissue beyond the rectum were found. There were no signs of either peritoneal or hepatic involvement, but it was obvious that removal of the rectum alone would not suffice. A left iliac sigmoid colostomy was performed.

About three weeks later a second operation was performed, under spinal, caudal and light general anæsthesia. This was an abdomino-perineal excision, with removal of the uterus and vagina.

The specimen shows the rectum and lower pelvic colon with an extensive ulcerated growth 4½ in. by 3½ in., almost encircling the rectum. From the anterior part of the crater a fistula runs into the vagina, invading its posterior wall. A very small uterus is seen above the infiltrated vaginal wall, firmly adherent towards the cervix.

The patient is doing her full work at the present time and there is no sign of recurrence.

(4) **Myxo-Fibroma of Mesentery.**—Patient, a man aged 62, had for some months had a feeling of heaviness and oppression in the abdomen. He had a large freely movable swelling in the abdomen.

Operation, 24.7.30.—Through a left paramedian incision a large tumour was delivered, and this was seen to arise from the mesentery attached to the intestine in the neighbourhood of the lower part of the jejunum. From ten to thirteen inches of small intestine were resected with the tumour and an end-to-end junction was made. Convalescence was satisfactory.

The tumour is solid, with a pinkish surface, and measures 9½ by 9 by 5 in. The mesentery of the small gut is closely adherent over part of its surface. On section a striated gelatinous structure is seen with definite fibrous septa separating lobules. A few hæmorrhagic areas are seen.

Microscopically, the tumour is of a loose, mixed myxomatous structure, supported by delicate strands of fibrous tissue. A definite fibrous capsule is seen with a few well-formed blood-vessels in the neighbourhood. The tumour is suggestive of a mesenteric fibroma with myxomatous degeneration.

(5) **Fibro-Sarcoma of Mesentery.**—Patient, an obese woman, aged 38, for several months had had attacks of abdominal pain. During the attacks a tumour was noticed in the epigastrium, but in the intervals nothing could be felt.

At operation a tumour was found in the region of the lower jejunum. It was attached firmly to the mesentery and was removed with eight or ten inches of small intestine. An end-to-end junction was performed. The gut was dilated above the tumour and was collapsed below it. Probably the weight of the tumour had established at intervals a condition of volvulus. Nothing of further interest was found except many large dilated veins over the surface of the mesentery in several places.

The tumour is dark purple in colour, with areas of plastic peritonitis on the surface. It is lobulated, and measures 3½ by 2½ by 4 in. On section several cysts are seen containing brownish fluid necrotic tissue and blood-clot. The solid parts of the tumour show necrotic areas.

Microscopically, spindle-cells with well-formed nuclei predominate and between them are areas of hæmorrhage. Formation of new blood-vessels is not apparent and some degree of necrosis and organization of blood-clot is present in parts. The tumour takes the form of a very cellular fibroma or fibrosarcoma, which, owing to torsion, shows hæmorrhage and necrosis throughout its substance.

(6) **Extensive Carcinoma of Colon.**—Patient, female, aged 48, and weighing 16 st., had for six months complained of anæmia, general loss of health and marked loss of weight. The bowels were becoming increasingly obstinate and blood was noticed in the motions. On examination, a large tumour was felt in the right loin, not adherent to the anterior abdominal wall, but only slightly movable.

At operation, 11.6.30, a large growth in the neighbourhood of the hepatic fixture was seen, involving the stomach and adherent to the surrounding structures. The cæcum was greatly dilated, and also invaded by growth, while œdema was apparent in all the structures affected. An ileo-transverse colostomy was performed with a side-to-side junction. Nineteen days later the abdomen was reopened, the part of the stomach affected was resected, and the freed cardiac end joined to the small gut by the ordinary Polya type of anastomosis. The duodenal stump was carefully closed. The peritoneum on the outer side of the right colon was mobilized and the small gut was divided about eight inches from the ileo-cæcal valve. The colon was also divided beyond the growth, and proximal to the anastomosis, and the mass was removed by dividing the respective mesenteries. The freed ends of colon and ileum were closed. A fæcal fistula formed about the fifth day, but the action through the bowel was satisfactory the whole time. This fistula closed spontaneously about ten or eleven weeks after the operation.

The specimen shows terminal ileum, with cæcum and appendix and ascending transverse colon, with an attached portion of stomach. The transverse colon is obstructed by an extensive new growth, 3 by 3 in., adherent to the cæcum, which it is invading, and a fistula is forming between the two parts of the colon. The cæcum is greatly dilated, owing to the marked degree of obstruction in the

transverse colon. The piece of the stomach adherent to the colon shows invasion of the outer coat, but no ulceration of the mucous membrane. Microscopically, the growth consists of a columnar-celled adenocarcinoma invading all coats.

(7, 8, 9) Three Cases of Œsophageal Diverticula Removed Successfully by Two-stage Operation.—(I) Patient, male, aged 71, for two years had complained of making a noise when he took food. Some time after a meal food tended to come back in a more or less unaltered condition.

Barium bolus showed that food was held up at the level of first and second thoracic vertebræ where the base of a large pouch was seen wedged in the thoracic inlet. Respiratory distress was occasioned before the sac filled.

Œsophagoscopy showed a narrow opening to the pouch which could not, however, be entered.

(II) Patient, male, aged 73, had been losing weight rapidly. He complained of dysphagia for years but had rapidly become worse three months before the operation. He was extremely emaciated and suffered considerably from regurgitation of food.

An X-ray diagnosis of carcinoma was made, but careful inspection followed and showed that an œsophageal pouch existed below the level of the aortic arch.

(III) Patient, male, aged 58, for twelve months had complained of discomfort on eating, and a certain degree of dysphagia. He had lost weight considerably. The first skiagram taken led to a diagnosis of carcinoma, but further skiagrams revealed a large œsophageal pouch extending just into the thoracic inlet.

Comment.—The symptoms and history of these three cases are similar and in each a diagnosis of carcinoma had been suggested at some time. The X-ray diagnosis drew attention to the smooth, centrally placed under-surface of the pouch which, as it filled, occasioned distress and dysphagia. In cases of carcinoma the under surface is not so regular and the ragged stricture may be seen; further, the axis of the dilatation does not correspond to the central axis of the body.

Œsophagoscopy was made difficult by the arrangement of the opening of the pouch, and as the pouch increased in size the œsophagus tended to be more and more difficult to enter. On the other hand, as soon as the pouch was freed the œsophagoscope passed straight down the œsophagus beyond the opening of the pouch without any difficulty and there was no sign of contraction at this site.

At operation it was remarkable how easily the pouch could be withdrawn from the thoracic inlet, and the largest one, which the skiagram showed to lie behind the arch of the aorta, occasioned no difficulty in this respect. The opening was apparently situated in the posterior aspect of the inferior constrictor close to its lower border and then the bulk of the pouch passed down on the left side. The second stage of the operation was performed between the muscular layers of the pouch so that there was no danger of breaking down granulation tissue outside this.

In all the cases healing took place without the formation of any fistula and the results from the patients' point of view have been extremely satisfactory.

Discussion.—Mr. JULIAN TAYLOR said Mr. Wilfrid Trotter had shown that two-stage operations for the removal of pharyngeal pouches were unnecessary, provided that in the dissection of the pouch every scrap of muscle tissue was preserved, and the opening subsequently closed by suture, with two layers of the preserved muscular coat stitched over the suture line of the mucous membrane.

Mr. J. B. HUNTER said that in order to avoid strictures when operating on pharyngeal pouches it was wise to put in an œsophageal tube, as this showed the surgeon at once whether or not he was taking away too much of the pharyngeal wall.

Section of Surgery.

SUB-SECTION OF PROCTOLOGY.

[*March* 11, 1931.]

DISCUSSION ON ULCERATIVE COLITIS.

Dr. Arthur F. Hurst

Nature of the Disease.

Sir Samuel Wilks, who in 1875 was the first to describe ulcerative colitis, pointed out that it was indistinguishable anatomically from dysentery. During the war I had frequent opportunities at Lemnos and Salonica of sigmoidoscoping patients with dysentery. I at once recognized that amœbic dysentery presented a quite characteristic picture, which bore no resemblance to that of bacillary dysentery, and that the latter was indistinguishable from the ulcerative colitis with which I was already familiar. That infection with *B. dysenteriæ* occurred in England was already well known from Eyre's investigations on "asylum dysentery." In 1912 Nabarro isolated the dysentery bacillus at the autopsy of a child who had been attending the Great Ormond Street Hospital for many years as a case of recurrent colitis. Since then he has found that not only many cases of summer diarrhœa, but many diagnosed as chronic colitis in small children are caused by the dysentery bacillus. It is easy to understand how adults may occasionally develop ulcerative colitis as a result of infection with the *B. dysenteriæ* from children with these conditions. In 1923 Dudgeon had isolated Flexner's bacillus from material obtained from the surface of an ulcer through a sigmoidoscope in two cases of ulcerative colitis, and in 1927 Hadfield isolated it from the swab from an ulcer in a case I sigmoidoscoped forty-eight hours after the onset of hæmorrhagic diarrhœa. In 1928 Thorlakson and Cadman of Winnipeg isolated the bacillus in material obtained by scraping the base of an ulcer with a sharp curette, in four out of five cases, though they had never before isolated it in stools or from ordinary swabs from the ulcer surface. Last year Knott isolated Flexner's bacillus, which was agglutinated by the patient's serum, from a swab obtained from the raw surface left after I had snared a polyp from the rectum of a woman, aged 39, who had had very severe ulcerative colitis since 1925, and who had developed two long strictures and multiple polyposis, although numerous examinations of stools and swabs taken from ulcers during the five years of her illness had only shown the usual organisms found in such cases.

It is well known how difficult it is to isolate the *B. dysenteriæ* from the stools of patients with typical dysentery in the tropics after the acute stage has passed. The vast majority of cases of ulcerative colitis which come under skilled observation

in England are already chronic, so that it is easy to understand how rarely the organism is isolated. In my only really early case it was isolated without difficulty, and Thorlakson's cases and the case I have just described show that it may be present in the depth of the lesion when it cannot be found in stools or swabs taken from the ulcers. These positive findings seem to me of more importance than many negative observations. The identical morbid anatomy and the response of many cases, especially early ones, to specific treatment with antidysenteric serum confirm the view, which was first suggested by Saundby in 1906 and by Hawkins in 1909 and which I have consistently held since the war, that the disease is a form of bacillary dysentery.

Achlorhydria was present in about 25% of my cases. This is an important predisposing cause, as the absence of the normal acid antiseptic barrier of the stomach allows organisms swallowed in infected water or food to reach the intestines.

Complications.

It is only in recent years that I have realized the frequency of certain serious complications of ulcerative colitis, which had never been recognized before the war. This is probably due to the fact that numerous severe cases, which would formerly have died, now survive as a result of better treatment; many recover completely, but others run a very chronic course, which gives time for these complications to develop.

Among 693 cases at the Mayo Clinic between 1923 and 1928 there were 69 with adenomatous polyposis, 59 with stricture, 26 with perirectal abscess, 18 with perforation and 15 with malignant disease, in addition to 30 with arthritis (Bargen). This agrees closely with my own experience of the relative frequency of these complications, except that I have never seen a case of perforation. Though the ragged polypoid tags of mucous membrane described by Dr. Cuthbert Dukes are often mistaken for true polypi, there is no doubt that true polypi also occur; some of those I have removed have been found on microscopical examination to be typical adenomata, and their X-ray appearance, which Dr. Briggs will show later, is identical with that of primary polyposis. In a few such cases the polypi have completely disappeared with deep X-ray treatment, but this should never be used until the primary ulceration has healed. It is most important to recognize that strictures may develop without any change in the symptoms; in chronic cases a barium enema should therefore be given from time to time. I have had three cases in which complete recovery followed a short-circuiting operation, without which death would certainly have occurred. Dr. Briggs will show radiograms of one such case in which there was stasis in the enormously dilated cæcum for seven days, although the patient was still having the usual severe hæmorrhagic diarrhœa, and of another case with an eleven years' history, in which the strictures were associated with polyposis. Symptomatic recovery was complete in both instances, and the former patient has now been completely well for six years.

I have seen two cases in which carcinoma apparently developed from polypi of the rectum following ulcerative colitis, and in another, carcinoma, polyposis and active ulceration were all present together. Anal infections are of great importance, as they may persist after the colitis has healed and lead to re-infection of the colon.

Diagnosis.

Direct examination of the mucous membrane of the rectum, which is almost always the part first involved and the last to heal, is essential for diagnosis and for guidance in treatment. A long proctoscope is easier to manipulate, for those with limited experience, than a sigmoidoscope; it has the advantage of bringing the

mucous membrane nearer to the eye, and the condition of the anal canal—a matter of considerable importance—can be more easily investigated. I have seen several cases of carcinoma of the rectum and pelvic colon, which had been treated as ulcerative colitis until I sigmoidoscoped them. I have recognized with the sigmoidoscope about half a dozen cases of amœbic dysentery in patients who had never been out of England and who, having hitherto failed to respond to treatment, recovered completely after twelve injections of emetine. I recently proctoscoped a patient who had been regarded as a case of ulcerative colitis of long-standing; the mucous membrane of the rectum was normal, the blood having come from hæmorrhoids, and the lumen was filled with effervescing fluid fæces, which indicated that the diarrhœa was due to carbohydrate intestinal dyspepsia; rapid recovery followed abstention from starch-containing vegetables.

Treatment.

Rest in bed, warmth, and a generous mixed diet, from which the skins and pips of fruit and fibres of vegetables are alone excluded, are essential parts of treatment. When anæmia is present, transfusion not only improves the general condition, but often greatly hastens the healing of the ulcers.

By absorbing gas, charcoal often makes the patient much more comfortable. Of the various drugs used locally, I have found tannic acid (1-2 gr. to 1 oz.) the most useful. If given after preliminary lavage with normal saline solution under low pressure, through a soft catheter introduced just beyond the anus, it reaches the cæcum and is generally just as effective as if given through an appendical or cæcal stoma. Quite recently I have been using hydrogen peroxide (2 dr. to 1 pint) without preliminary lavage, and results so far are very promising.

In the first case in which I used polyvalent antidysenteric serum in 1921 the result was little short of miraculous. A young man who was almost moribund after being very ill for over a year, and in whom no improvement had followed an appendicostomy, recovered completely in a fortnight; five days after the first injection the sigmoidoscope showed that the innumerable ulcers seen a few days before had vanished, and nine days later the appearance of the mucous membrane was absolutely normal. Since then I have had a number of cases in which a dramatic recovery has taken place, and my colleagues, Dr. Fawcett and Dr. Ryle, and Jerwood, Brindon Brew, and many others have had similar experiences. Rapid recovery is most likely to occur in early cases, but it is occasionally observed in very chronic ones. More frequently the serum produces a certain amount of improvement, with the result that other treatment leads to recovery more rapidly than it would otherwise have done. In a small number of cases, especially very chronic ones, the serum appears to have no effect.

I have never seen the slightest benefit follow any form of vaccination, and in some cases the local condition has been definitely aggravated.

In my experience the mortality of ulcerative colitis is extremely low. We have had an average of two severe cases a year at New Lodge Clinic since 1921 without a death. Complete recovery may occur after very long periods of treatment, and in cases which do not respond to serotherapy as much as a year or two of continuous treatment may be required. There is also an unfortunate tendency to relapse. The danger of this is much reduced if treatment is continued until the sigmoidoscope shows no trace of inflammation, even if symptoms have already disappeared for some weeks. Such associated conditions as oral and pharyngeal infections and anal complications must be treated, as a relapse may follow an acute sore throat or the development of a peri-anal abscess or a fistula-in-ano. The patient should always take sufficient paraffin to keep his stools soft; if achlorhydria is present the

associated gastritis should be treated, and, if the secretion of acid does not return, the patient should take hydrochloric acid for the rest of his life.

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Dr. P. J. Briggs showed a series of lantern slides to demonstrate the value of radiography in determining the extent of the disease (cases I and II) and the presence of strictures (cases III, IV and V) in cases of ulcerative colitis.

FIG. 1.

Case I.—A woman. Fig. 1 shows absence of haustration in the pelvic and descending colon with weak haustration in the transverse and ascending colon and cæcum. There was slight incompetence of the ileo-cæcal sphincter.

Case II.—A man, aged 24. Fig. 2 shows a well-marked constriction in the iliac colon with lack of haustration in the pelvic, iliac and descending colon. The transverse colon was

FIG. 2.

normal. The ascending colon and cæcum showed the ragged, "moth-eaten" appearance, to which Dr. Graham Hodgson has already called our attention. The ileo-cæcal sphincter was incompetent.

Case III.—A girl, aged 21. Fig. 3 shows well-marked obstruction to the opaque enema in the descending colon. Fig. 4 is from the same case three-quarters of an hour later: the opaque fluid can be seen filtering through the constriction and filling the descending colon. Fig. 5 is a combination of an opaque meal taken 96 hours earlier, and an opaque enema, and shows the enormously dilated ileum, cæcum and ascending colon, to which Dr. Hurst has referred; there was a long stricture at the hepatic flexure and the whole of the transverse colon was replaced by a tube of very small lumen with irregular outline. In spite of over 96 hours' stasis in the proximal colon, severe hæmorrhagic diarrhœa was present. The patient had an ileo-sigmoidostomy performed and has now been well for six years.

Case IV.—A woman aged 51. Fig. 6 was taken in 1924, and shows the more common type of short stricture in the pelvic colon, complete absence of haustration in pelvic, descending and left half of transverse colon with the beginning of a long type of stricture in the right half of the transverse colon. I re-examined this patient yesterday, seven years later (fig. 7): the narrowing in the right half of the transverse colon is less and haustration has reappeared from the cæcum to half way down the descending colon. There is a long stricture in the iliac colon, which did not, however, cause delay to the passage of the opaque fluid.

FIG. 4

FIG. 3.

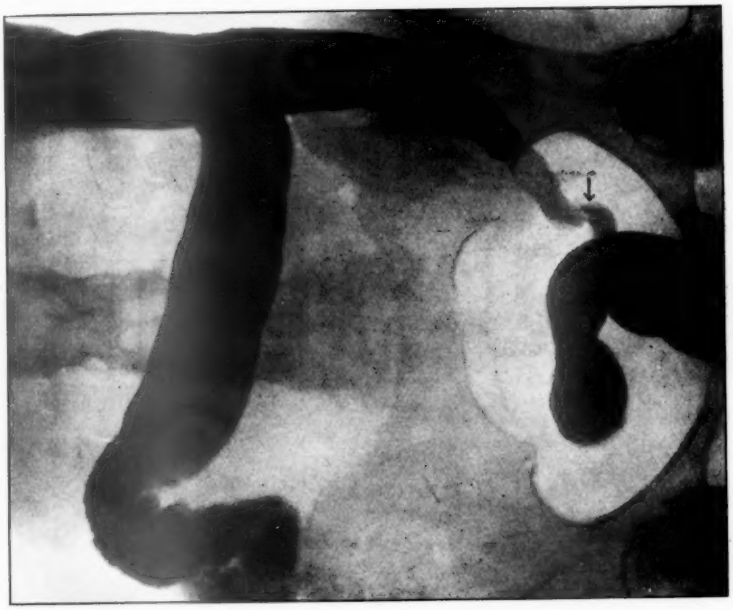

FIG. 6.

FIG. 5.

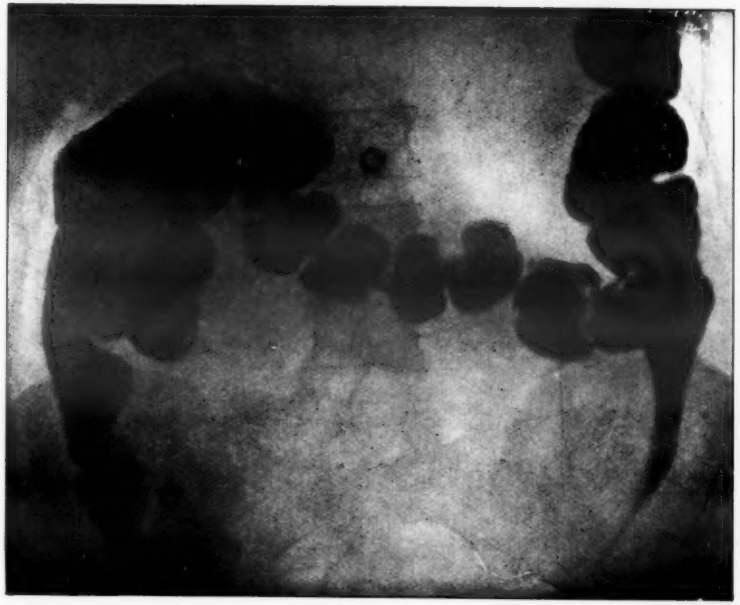

FIG. 7.

FIG. 8.

FIG. 9.

Case V.—A woman aged 40. Fig. 8 shows a well-marked short stricture proximal to the hepatic flexure. The remainder of the colon is narrow and shows lack of haustration. There are several translucent areas around the splenic flexure and in the descending colon which are probably due to the presence of polypi, some of which were seen on sigmoidoscopic examination. Fig. 9 is of the same patient after ileo-sigmoidostomy. An opaque enema was given and passed readily into the ileum; the extremely narrow colon from the cæcum to the pelvi-rectal flexure can be traced.

Dr. Cuthbert Dukes: *Pathology.*—Chronic ulcerative colitis begins as an acute inflammation of the mucous membrane of the colon, leading to patches of localized necrosis, followed by separation of sloughs and superficial ulceration. In severe and fatal cases the ulceration is often most conspicuous opposite to the longitudinal muscle bands of the colon, between which is seen a thin strip of irregular fringed surviving mucous membrane (see fig. 10). If the ulcers heal, ragged polypoidal tags of mucous membrane remain in about 10% of cases. These are not true adenomatous proliferations, and the tendency to carcinoma (assessed at 2·6%) is much less than in polyposis intestini or multiple adenomata [13]. Other sequelæ are stricture consequent on fibrosis, in 8·5%, and perforation in 2·6% [8]. In spite of the intestinal ulceration urinary infections are not more common than amongst the general population.

Ætiology.—Of the four theories which postulate a specific ætiological agent as the cause of the disease, none provides a completely satisfactory explanation.

(1) The claim that the disease is related to bacillary dysentery [18] is discounted by the almost universally negative bacteriological and epidemiological evidence, the absence of agglutination and the uncertain effect of antidysentery serum.

(2) The theory that ulcerative colitis is due to *Entamœba histolytica* is not

FIG. 10.

A portion of the colon from a fatal case of chronic ulcerative colitis. In the upper drawing the intestine has been opened up and spread out to demonstrate the linear character of the ulceration and irregular tags of mucosa. The lower drawing is of a transverse section of the intestine and shows the relation of the ulceration to the longtitudinal muscle bands.

supported by laboratory evidence or by the effects of emetine therapy, but it is certainly true that cases of amœbic dysentery have been wrongly diagnosed as ulcerative colitis because the stools were not examined microscopically.

(3) The diplostreptococcus which Bargen regards as the cause of the disease can certainly be cultivated from the ulcers, but it is found also in other types of

ulceration and in normal people. Although intravenous injections of rabbits with Bargen's coccus causes diarrhœa, with blood and mucus in the fæces, the course of the experimental disease does not resemble human ulcerative colitis and in rabbits similar symptoms follow inoculations with other bacteria. Bargen's diplococcus and similar types of fæcal streptococci [1, 12, 17] are probably secondary invaders, the ulceration being first caused by some other factor. Vaccines and antistreptococcal sera have often been reported as useful in treatment [3, 15, 16, 21, 6], but this is to be attributed only to the more rapid healing of the ulcers following immunization against secondarily infecting organisms.

(4) The theory that the disease is due to an avitaminosis is not supported by clinical experience.

Until more definite evidence is obtained, I adopt the view that patients suffering from ulcerative colitis are born with inferior intestinal organs, showing an unusual susceptibility to trauma and diminished resistance to bacterial infections. Subjects needing further investigations are the alleged infectious nature of the disease, the patient's psychological outlook [19] and the resemblance to the ulcerations of uræmia, bismuth, mercury and arsenic poisoning.

Value of laboratory tests.—The part which the pathologist can play in the diagnosis and treatment of the disease may be defined as follows: The fæces should be examined in order to confirm the presence of blood and pus and to exclude amœbic and bacillary dysentery and any other defined infection. Observations should be made on the relative proportions of streptococci and staphylococci, the presence of late and non-lactose-fermenting bacilli and hæmolytic bacteria. A good deal more can be done if the pathologist has a sample of the patient's blood and can collect his cultures from an ulcer through the sigmoidoscope. Several different colonies of bacteria from the ulcers should be tested for agglutination by the patient's serum. I only recommend an autogenous vaccine when the agglutination test is positive for bacteria from an ulcer. In some cases this test may show the secondarily invading bacteria to be streptococci, and in other cases staphylococci and hæmolytic strains of *Bacillus coli*.

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Mr. J. P. Lockhart-Mummery: *Surgical treatment and after-effects of ulcerative colitis.*—The great majority of cases of ulcerative colitis, apart from tropical dysentery, are due to an infection of the mucous membrane of the colon by streptococci, very commonly the *Streptococcus viridans* or *fæcalis*. A few cases are

due to tuberculous infection, some to infection with the *Diplococcus pneumoniæ*, and occasionally other organisms are found as the primary infecting agent.

Every grade of severity of the disease is met with, depending doubtless upon the specificity of the original infection and the amount of individual resistance of the patient. Mild cases are not uncommon, and these can often be effectively treated by non-operative methods, though I have seen cases in which a mild infection has suddenly flared up and become septicæmic.

We are now more particularly discussing the type of case in which there is a serious infection of the large bowel and in which a sigmoidoscope examination shows extensive ulceration. It has been recently stated in the medical press that a sigmoidoscope examination of the bowel is not necessary in the treatment of ulcerative colitis, and this strikes me as a retrograde and pernicious doctrine. Examination of the discharges from the ulcers is not good enough evidence on which to found a diagnosis, nor does it give sufficient information as to the severity of the disease. The sigmoidoscope is required in order not only to make a differential diagnosis from cancer, but also to watch and check the results of treatment. The sigmoidoscope can be used to examine the mucous membrane of the colon in all cases of ulcerative colitis, without causing any pain or necessitating an anæsthetic, and without the slightest danger. It has been so used at St. Mark's Hospital for years, and although, admittedly, a certain amount of skill in using the instrument is necessary, this can—and should—be easily acquired.

My experience of the treatment of ulcerative colitis, which is fairly extensive, is that appendicostomy is curative, provided it is performed early, that is to say, before the bowel has been severely damaged. At St. Mark's Hospital we have large numbers of these cases and in the course of the last few years we have tried all the different treatments for the condition, but we have always come back to appendicostomy as the one method to be relied upon, not only to save the patient's life, but also to prevent frequent recurrences. Ulcerative colitis is one of those diseases, like tuberculosis, which has a great tendency to relapse. Only recently I saw a patient upon whom I had performed appendicostomy on account of ulcerative colitis seven years ago. She recovered from the original attack and allowed the opening to close, but the condition relapsed and for five years she was treated by various methods and at various institutions, but was quite unable to regain her health. She asked me to reopen the appendicostomy as it was the only means of preventing recurrences, and I did so, and she was almost immediately free from symptoms and has since remained well.

Unfortunately there seems to be an idea prevalent that ulcerative colitis should be treated by lavage and medical methods, and that operation should only be resorted to when these methods have failed. I am sure that this idea is wrong; it results in too long delay before operation, and the patient, in consequence, is not afforded the best chance of recovery. When performed as a last resort, appendicostomy must of necessity often fail to cure, but in my experience it very seldom fails when it is carried out during the early stages.

An important point in technique is that the appendix should not be opened until the skin wound is healed, otherwise severe infection of the wound is likely to occur from the infected mucous membrane of the appendix.

With regard to the after-results of ulcerative colitis: as already stated, one of the outstanding features of its diseases is its tendency to recur, often after long intervals. This has to be taken into account when treating cases. When patients are treated by medical means only, it often results in their being laid up in bed or undergoing treatment for many months in the year, and this in these busy days means that they are seriously handicapped. I have had to operate in many such cases and perform appendicostomy because the patients could not afford the time for the long and tedious treatments which were necessitated by the frequent

recurrences. There is apparently no means of preventing recurrence, but if each recurrence is promptly and adequately treated, the tendency, in time disappears.

If an appendicostomy is performed, the opening should not be closed until the patient has been for a full year without treatment and without any recurrence. Fortunately the opening is very easily reopened, even if the patient has allowed it to close.

What, in my experience, has been a rare after-result, is stricture of the colon, but within the last six months I have seen two very serious cases due to this cause.

(1) In the first case, that of a woman aged 26, who had suffered for eight years, I suspected the possibility of a stricture because the patient had persistent diarrhœa, in spite of the fact that a sigmoidoscopic examination showed no signs of any ulceration. An X-ray examination revealed a long and narrow stricture in the transverse colon, and another in the descending colon. I opened the abdomen and found the colon almost completely occluded for 4 in. on the right side of the transverse colon and a severe stricture in the descending colon. There was dense cicatricial tissue, and it was obvious that nothing could be done with the damaged bowel. I therefore performed a lateral anastomosis between the ileum and the pelvic colon. The patient made a good recovery.

(2) The other patient had only been ill for 2½ years, but had had a very serious attack. Both he, and the previous patient, had been treated by medical means only. An X-ray examination of this second patient showed a stricture in the splenic and descending portion of the colon.

I think that if some of the old cases of this disease, in which the symptoms refuse to disappear—in spite of the fact that they have been thoroughly treated and that the sigmoidoscope does not show any serious degree of ulceration—are examined by X-rays, a similar condition will be found.

Other late results, which I believe are rare, are joint changes and septic arthritis. I should have expected these to be common complications, but I have not found them so.

Liver abscess, which is such a common complication of amœbic dysentery, seldom occurs in ordinary ulcerative colitis.

Perforation of the bowel wall is a well-known complication, but only occurs during the acute stage of the disease. It is generally fatal, as patients suffering from acute ulcerative colitis are in the worst possible condition for undergoing the operation necessary to deal with the perforation.

An important point with regard to the pathology of ulcerative colitis is the relationship between this condition and colitis polyposa. It has been stated that multiple adenomata of the colon may result from ulcerative colitis, but, as I pointed out in a paper read in 1909, the condition following ulcerative colitis is one of granulomata, not of adenomata, and bears no relationship to the disease of adenomatosis. The apparent adenomata found in ulcerative colitis are really isolated inflamed islands of mucosa left between areas of ulceration.

Dr. H. Letheby Tidy said that he had participated in the discussion which took place on this subject twenty-three years ago. He was then responsible for the statistics at the London Hospital, and was able to confirm the statement that the results were, at that date, appalling.

He was particularly interested in this condition during the late war, when he was in a dysentery hospital, and he there grew into the methods which he still employed. Since the war he had had 27 cases in private practice, in which there had been three deaths, one from coronary thrombosis in a man older than the ordinary type of case. Five years ago he ceased doing sigmoidoscopy, and since then he had had 13 cases, with no deaths. He considered that for the treatment of this disease neither operation nor sigmoidoscopy was necessary.

In treatment there were certain principles which must be adopted: the patient must be well fed, must be kept warm, and must take fluid by the mouth. There

were certain things which must not be done: injections of morphia must never be given, nor must medicated enemata be given in the acute stages, or in the early stages of chronic cases. The daily enema must never be adopted. If these points were attended to, whatever line of treatment was followed, the subject would be removed from the appalling mortality which had been associated with it in the past, when medical treatment depended upon starvation, injections of morphia, and daily medicated enemas,—treatment which would cause ulcerative colitis in practically every healthy person.

He (Dr. Tidy) adopted three stages of treatment by the rectum—(1) starch and opium, (2) colonic washes, (3) in a late stage, medicated enemas. For the first he gave 3 oz. containing 20 to 30 minims tincture of opium; these could be given up to five a week, and never more than three consecutively. He continued this course until there were not more than five stools a day. The colonic wash was a simple salt wash—two pints. That was given every other day, and continued until the stools were consistently less than five a day. That might be a matter of a long time; it might be necessary temporarily to go back to the starch and opium enema. The medicated enema was used only when the stools numbered less than five a day. He gave 25 oz. containing 20 gr. of albargin—never more than three a week, not more than six in a fortnight, and with a week's interval before the course was renewed.

[Dr. Tidy showed on the screen the temperature chart of the last case of the kind he had had under treatment in St. Thomas's Hospital. The patient was a woman aged 22 whose illness had begun ten days previously. Before admission she had been passing from ten to twenty stools a day, and they had been intimately mixed with blood. On admission, her temperature was 103° F., pulse 140. The condition was undoubtedly ulcerative colitis. Her normal weight was 9 stone 5 lb.; four days after admission it was 8 stone 7 lb. She was weighed again two weeks later, and then was 8 stone. Starch and opium enemata; and at the end of three weeks the temperature was approaching the normal; she was passing a little blood, and pulse was down to 100. She had another course of starch and opium enemata, and the stools were reduced to two or three a day. Then colonic washes were begun. In seven weeks the chart showed the frequency to be one or two stools daily.]

Treatment by the mouth was of little importance, unless in special circumstances.

With regard to after-treatment, there were two special difficulties. One was constipation, for which he preferred to use paraffin. The other was diarrhœa. Some looseness of motions might continue for months after it was necessary to have strict treatment. He gave one starch and opium enema and one colonic wash a week, and that could easily be provided.

He had found no effect from the use of vaccines. He regretted that he had not had the good fortune which Dr. Hurst had had with serum, though he had tried it several times, but he was prepared to continue to try it, as he was sure some of these cases must be of the same type as bacillary dysentery. He had no experience of ionization.

With regard to surgery, he did not see that it offered any improvement on the results which he had had in recent years; yet he recognized that the work of Mr. Lockhart-Mummery had been largely instrumental in rescuing this disease from the reproach of an 80% mortality. He had put forward evidence—which he would not now repeat—that sigmoidoscopy was incompatible with treatment by enemata, and it was not necessary for diagnosis and watching progress. He had not seen at autopsies that mistake was made clinically between ulcerative colitis and neoplasm. Given four or five days' observation in a hospital or in a nursing home, diagnosis was easy. If a mistake was made it was generally in taking a case of light diarrhœa to be one of severe ulcerative colitis.

Dr. Graham Hodgson: The radiogram (see fig. 11) illustrates the condition in the case described by Mr. Lockhart-Mummery, and is typical of the appearances seen in an advanced case of chronic ulcerative colitis.

FIG. 11.

There is an entire absence of haustration in the distal colon and numerous small irregularities and filling defects are seen throughout its entire length, this being due to fibrosed tags of mucosa. The barium enema runs rapidly through the rigid colonic tube, and under the screen one gains an impression of the rigidity of the colonic wall when one palpates it. A band-like constriction can be seen in the distal part of the transverse colon. This was proved not to be due to spasm by using the dual exposure method, which showed only a single outline through this area thereby proving that peristalsis is inhibited as the result of thickening of the bowel wall.

Dr. F. J. Poynton said that he probably had a more intimate acquaintance with this disease than any of the other speakers, because in 1893, when he was a student, he had such a severe attack of acute ulcerative colitis that his case was published in the *Lancet* as one of the first instances of recovery on record. Nervous strain was, in his opinion, a predisposing cause of the condition. He was thankful that the treatment in those days included neither the passage of a sigmoidoscope nor surgery, for, in the event of either, he would probably have been a dead man. His hospital experience led him to ask how a sigmoidoscope could indicate whether a case was cured or not, unless it was possible by its use to see as far as the cæcum since the ulceration extended, in bad cases, throughout the colon? No speaker in the discussion had as yet referred to a painful complication that might follow this disease, namely, spasm of the colon. The best remedy in his (Dr. Poynton's) experience for that was morphine. Treatment seemed to him a matter of individual experience.

The physician obtained his best results with medicines, the surgeons with surgery, the specialist with bowel-washing and other methods. He himself had had some great successes, even in bad cases with hæmorrhage, by highly skilled nursing, most careful dieting with liquid food, opium and bismuth by the mouth, and also opium enemata. One remedy which he had found most useful both in adults and the rare cases in childhood was kaolin.

Dr. L. P. Garrod said that recently he went through the records of examinations by sigmoidoscopy and swabs of cases of the condition, in St. Bartholomew's Hospital chiefly, in the last two or three years, and the results were as follows: Of cases admitted with the diagnosis of ulcerative colitis, four proved to be cases of amœbic dysentery. In some of them the condition had existed for some time, in one of them for three years. None of the patients had dysentery bacilli in the stools. About twenty had various bacteria, coliform bacilli of aberrant types, which might or might not be significant. Eleven out of seventeen cases showed the presence of Bargen's coccus, and that was the organism to which he desired to refer.

As Dr. Dukes had mentioned, Bargen found that this coccus was capable of producing lesions in rabbits. He (the speaker) agreed with Dr. Dukes that that observation was of no significance. Bargen found the coccus in 80% of a large number of cases when the examined material was obtained from the ulcer itself. He cultivated it in a complex medium, a method which he (the speaker) regarded as unnecessary. One of the constituents of that medium was brain, and it was difficult to see why brain was necessary for an organism grown in the colon. He (Dr. Garrod) had found it easy to grow the organism in dextrose broth rendered anaerobic by the addition of a paraffin seal. The reason it grew there and not on other media was its great avidity for sugar. The anaerobic conditions did not affect its growth, but they affected the growth of the other bacteria. When a primary culture had been obtained in that medium, it could be isolated by plating. The organism which he had grown in eleven cases was identical with that of Bargen, though he had not had a culture from Bargen's laboratory with which to compare it.

Three reasons for regarding this organism as of considerable significance were: (1) It could only be found by this method in material obtained from the actual ulcer; if ordinary fæcal matter were cultivated by this method the organism did not appear. (2) The fact—not recorded by Bargen—that it could be demonstrated in great numbers in direct films from the muco-pus of the ulcer. (3) Out of eight cases in which he had carried out an agglutination test—using first the patient's serum, then his own—the patient's serum agglutinated it in three, and his own did not. That showed that the organism played a part in this disease, though perhaps only a secondary one.

It was worth while, in all cases of ulcerative colitis, to carry out an exhaustive bacteriological examination. The classification of the disease into different types had proceeded as far as it could on clinical grounds, with or without the sigmoidoscope, and it was evident that certain cases responded to certain treatment and others did not. Progress was now more likely to be made by classifying ulcerative colitis into types according to their bacterial content, and relating treatment to those types.

He had known two cases in which the disease was tuberculous. It was possible to find tuberculous ulcers in the lower part of the descending colon when there was no other sign of tuberculosis in the body.

Sir Charles Gordon-Watson said that year in and year out, he had never been without one or more cases of ulcerative colitis in his wards, and every form of recognized treatment had been tried there. His general impression as a result was that some cases did well, others did not, and that the particular treatment which

was carried out did not seem to matter much, so long as it was on sound general lines. When Dr. Hurst first recorded his results with anti-dysenteric serum he, the speaker, tried it. There was one dramatic result, a brilliant cure, with that serum. Yet, though he had tried it on a large number of cases since, he had never satisfied himself that there had been much benefit from it. The case which had responded so well to it relapsed, as most of these cases did, after a year or two, and when the patient came back to hospital she did not respond to antidysenteric serum.

Except in the mild cases, he (the speaker) always performed appendicostomy; he did not think one could deal with the proximal colon adequately by the rectum. He regarded appendicostomy as a definite life-saving measure in many cases.

With regard to irrigation, he had used barium sulphate solution for the irrigation of the colon from the appendicostomy. He had one case now under treatment which had been very bad, but was improving rapidly with barium sulphate washes and periodic blood transfusions. He laid stress on the value of the latter. If patients in chronic cases had a blood-transfusion every four weeks, they improved. If after improvement they lost a little ground, a further transfusion brought benefit again.

Sir Charles Gordon-Watson demonstrated, by means of films, post-ulcerative stricture. The first showed absence of claustration, with a very tight stricture close to the splenic flexure, and a less advanced stricture in the pelvic colon. There was also a stricture of the rectum which had existed for five years, and from time to time had to be dilated. The next film was from the same case, taken after rest and treatment, and showed that the strictures which appeared to be organic in the first film were in part due to spasm. Another film showed tuberculous ulcerative colitis, with three tuberculous strictures in the cæcum, the ascending and transverse colon. These cases did not show symptoms like those of ulcerative colitis, and the condition was not easy to diagnose. This patient travelled from hospital to hospital for sixteen months. First she was treated for gastroptosis, then for endometritis, then for nephritis, and in his (the speaker's) own hospital she came into the gynæcological department, where her case was diagnosed provisionally as one of tuberculous disease of the tubes and ovaries, as the cæcal tumour was in the pelvis. The specimen which he showed had been removed by resection and anastomosis, and he showed it because such a condition was rare.

Dr. Julius Burnford said that he had had about fifty cases of ulcerative colitis, many of which had been to other London hospitals. He thought that some cases of this condition were curable and others incurable. Incurability was understandable when one considered the anatomical condition, because there was such a great destruction of the mucosa. He treated the condition by ionization. He had recently published an analytical review of 28 cases,[1] and since then he had been successful with additional cases, bringing the number to 48. In four or five of these cases the patients had died. He had found the results of ionization very good. If in cases having medical treatment, benefit did not occur in three weeks, it was right to call in the surgeon and ask him to put the colon at rest. It was an important matter to determine when the physician should ask the help of the surgeon.

His own routine was to put the patient to bed, give castor oil twice a week, then ionize with ½% to 1% zinc sulphate by the lower bowel, giving a generous diet. As a large percentage of cases had achlorhydria, he gave hydrochloric acid. In fifty cases he had 80% cures. After-treatment consisted in dealing with the anæmia, and transfusion was beneficial.

He did not agree that ulcerative colitis was a specific infectious process,

[1] *Brit. Med. Journ.*, 1910, ii, 640.

In a few of his cases the patients had had arthritis. In one of the fatal cases there were ulcerations in the appendix. In another fatal case an ulcer perforated, and the patient died from a low-grade peritonitis.

As to the ionization current not passing along the bowel, Dr. Carter Braine had stated that a small amount of current reached the cæcum.

Dr. W. Kerr Russell: It might be advantageous to consider the various physical methods of treatment which have been used at different times in ulcerative colitis.

The use of diathermy has been advocated, the cylindrical active cathode being placed in the rectum, the inactive being applied round the waist in the form of a lead belt. The greatest concentration of current occurs in the rectal and sigmoid regions. The maximum current strength is generally one ampere, and treatment is usually given for twenty minutes. As is well known, the diathermic current causes internal heating and improved lymph and blood circulation, and has a vitalizing effect on the tissue cells and a marked antispasmodic effect on muscular tissue.

Ionization treatment has also been applied in cases of ulcerative colitis. Whenever possible the lower bowel is first washed out with a warm water enema, and large pad electrodes are applied to both the lumbar and abdominal regions. Both these electrodes are connected to the negative pole of the galvanic apparatus. The positive electrode consists of a spiral wire, which is inserted into a thick rubber tube, a foot long and closed at one end, but having a lateral opening. This rubber tube is connected with a douche can containing about two pints of a $\frac{1}{2}$ to 2% solution of zinc sulphate at a temperature of 104° F. After about a quarter of the fluid has been slowly run into the bowel, the current is switched on and the strength gradually increased to a maximum of from 15 to 20 milliamperes. Treatment is generally given for fifteen minutes and, provided that there is no discomfort, all the fluid is allowed to flow slowly into the bowel. The treatment is repeated once or twice a week.

Another treatment, which has been used successfully in early cases of ulcerative colitis is colonic irrigation. There are two methods of colonic lavage, which have great advantages over the Plombières system. One was evolved by Von Borosini and the other is known as the "Studa Chair" method. They are so fundamentally alike that they may be described together. In both methods a rectal catheter has been designed which remains in the rectum throughout the administration of treatment, and is not dislodged when defæcation takes place. In the case of the Studa Chair the patient sits on a rubber ring cushion. The rectal catheter is L-shaped. The vertical limb which is inserted into the rectum is $3\frac{1}{2}$ to 5 in. in length, and 6 mm. in diameter, and is connected with the 7-inch horizontal limb by means of a ball-and-socket joint, which allows considerable movement. The free end of the vertical limb is dome-shaped and there are four lateral openings. The catheter is introduced into the anal canal and is kept in position when the patient sits down, by pressure on the horizontal limb. The catheter is connected by means of a rubber tube with a tank of about eight gallons capacity, filled with a slightly hypotonic solution of sodium chloride at a temperature of 104° F. The bottom of the tank is fixed three feet above the chair seat.

A valve controls the rate of flow of the irrigating fluid through the catheter into the rectum. Evacuation occurs when the intra-colonic pressure has become sufficiently great; usually this is when half a pint of fluid has entered the bowel. If treatment is continued for half an hour, from fifty to sixty evacuations occur. At first the irrigating fluid flows into the rectum and sigmoid flexure, but after about ten minutes the transverse colon is reached and its contents gradually evacuated, and finally the irrigating fluid finds its way down the ascending colon into the

cæcum; a normal ileo-cæcal valve prevents the fluid from entering the small intestine. I have recently had radiographic proof of this. The treatment thoroughly cleanses the lumen of the large bowel, removing all residual matter in a gentle way. Profuse diuresis invariably occurs. Certain antiseptics, such as dimol or monsol, can be added to the irrigating fluid, or such antispasmodics as kamillosan, etc. Dimol solution, used in this way, appears to destroy intestinal micro-organisms. Treatment is generally given every other day. Oxygen foam is sometimes added to the irrigating fluid; this foam is formed by bubbling oxygen through a special distributor immersed in a solution of warm water containing a little ext. quillaiæ liq. B.P.C., the distributor being enclosed in a special metal container. The foam rises to the surface of the water in the bowel and gently fills the cavity.

The physical properties of the foam bring it into intimate contact with the mucous membrane of the bowel, and all the folds and pouches are entered, oxygen being liberated. The mucous membrane is in this way thoroughly cleansed.

Various medicaments can be added to the liquid from which the foam is produced, and they are then present in the foam in a finely dispersed state.

The President said he was sorry to hear from medical colleagues that the sigmoidoscope was no longer useful, because it was very difficult in certain cases to diagnose ulcerative colitis from other conditions, especially carcinoma of the colon. He remembered the case of a man with chronic nephritis, with acute exacerbations of cardiac failure, who had begun to pass a large quantity of blood and mucus per rectum. The picture was that of an ulcerative colitis—which was well known as a terminal condition in chronic nephritis. The sigmoidoscope, however, showed a carcinoma of the pelvic colon. Without a sigmoidoscopic examination this patient might have been treated for ulcerative colitis.

He (the President) was in favour of appendicostomy in certain cases, but he had noticed that though one performed appendicostomy and the patient recovered, and felt very well, if one examined with the sigmoidoscope a short time later, the picture looked the same as previously. He had a patient who had been irrigating through an appendicostomy for five years. She was better every time he saw her. She had passed no blood or mucus, but there was the same picture, a raw surface which bled easily, with a granular condition of the mucus membrane. That had been his experience in a fair number of cases. He could have claimed a cure in many cases but for this subsequent sigmoidoscopic examination. In another patient who had been washing herself out for five years he thought everything was going well, and the mucous membrane looked normal. He closed the appendicostomy, but in a few months the condition started again, and the sigmoidoscopic appearances were very disappointing.

JOINT DISCUSSION No. 3.

Section of Surgery and Section of Pathology.

Chairman—Mr. C. H. FAGGE, M.S. (President of the Section of Surgery).

[*February* 4, 1931.]

DISCUSSION ON THE INDICATIONS FOR AND THE VALUE OF THE INTRAVENOUS USE OF GERMICIDES.

Mr. V. Zachary Cope: To avoid discussion at cross purposes I will first define the words "germ" and "germicide" in the sense in which I shall refer to them in my remarks.

By "germ" I indicate any pathological micro-organism, whether protozoal or bacterial: by "germicide" I mean any substance of known and fixed chemical composition which will kill germs either directly, when brought into contact with them, or indirectly, by unfavourably affecting their environment in the body. It is impossible to get a broad view as to the possibilities of germicides without considering their effect on the protozoa, and if we limit our discussion to the direct bactericidal effect of germicides we must omit some important and relevant data.

The destruction of pathological micro-organisms by the intravenous injection of a germicidal drug would appear to be a desirable procedure, on account of the speed and certainty with which all parts of the infected host can be reached. For the method to be indicated one should be dealing with a drug of certain or presumed efficacy, and of small toxic action upon the host in the doses used, and it must be assumed that administration of the drug by the alimentary or subcutaneous routes is either contra-indicated on account of the irritant action of the substance, or rejected because of slow absorption.

Presumption as to the efficacy of the drug may be obtained from experiments either in test-tubes or in animals, but there can be no valid and conclusive proof other than the clinical test in the human subject. (Noguchi showed that salvarsan was ten times as lethal to the Leishman-Donovan body as was tartar-emetic in vitro, but in the human body only tartar-emetic had any curative value.)

Micro-organisms or germs may be of animal or vegetable nature—protozoa or bacteria. A protozoon is in structure more nearly allied to the cells of the body than is a bacterium, and reason might have suggested that it would be more difficult to find an innocuous germicide for protozoa than for bacteria. Actually, the triumphs of intravenous therapy have been chiefly seen in the treatment of protozoal infections by four drugs or groups of drugs.

Arsenic compounds	Syphilis Relapsing fever Frambœsia	Spirochætes
	Sleeping sickness.	Trypanosomes
Antimony compounds	Kala-azar Baghdad boil	Leishman-Donovan body
Emetine	Amœbic dysentery and hepatitis.	*Entamœba histolytica*
Quinine compounds	Malaria.	Hæmatozoon malariæ

Everyone knows the wonderful effect of these drugs on patients suffering from the disease for which each particular drug acts as a specific. Most of them have a rapid killing effect on the organisms and clinically there is almost universal agreement as to their efficacy. The intravenous route is the method of choice in

the case of the arsenic and antimony compounds but only in urgent cases is it necessary to give emetine or quinine directly into the veins.

In passing, it is worth while remarking that there is still some doubt in bacteriological circles as to the proper description of the syphilitic organism. Its reaction to drugs would suggest that it belongs to the protozoa rather than to the bacteria.

For many years there was doubt as to the exact action of emetine in the body, whether it acted directly or indirectly upon the entamœba. It was for a long time asserted by experienced experimentalists that it had no direct killing action on the amœba. The most recent authoritative work, however, by Laidlaw, Dobell and Bishop, proves that with a simple liquid medium, a solution of emetine, 1 in 5,000,000, is lethal for all strains of *Entamœba histolytica* in vitro within four days, provided that the medium does not become too acid. This great potency of emetine may be altered by a comparatively small variation in the reaction of the culture medium. We accept the conclusion of these workers that emetine has a direct germicidal action on these amœbæ, and think that these experiments throw light upon the occasional discrepancy between laboratory and clinical findings.

When we come to consider the bacteria, the question of intravenous injection of germicides is not on so sure a foundation. The work of Fleming appears to prove conclusively that none of the ordinary antiseptics have any direct bactericidal effect when introduced into the blood-stream. The experimental work of Morgenroth, however, shows that it is possible to obtain a drug that will kill bacteria without unduly damaging the animal, so that we may look forward to obtaining some substance which may be of direct germicidal value.

On the clinical side various claims have been made as to the bactericidal effect of certain drugs introduced intravenously. Some of these claims appear to have very good foundation, and one must presume that the drugs in question act indirectly by producing in the host some change which is inimical to the life of the infecting organism. Other claims—the majority—appear to rest upon a mass of unjustifiable presumptions.

Let us briefly survey the attempts which have been made to find a safe and efficacious intravenous remedy for various bacterial diseases.

Anthrax	Salvarsan (Ehrlich)	Ethylhydro cuprein hydrochloride
Pneumococcus	Optochin (Morgenroth)	
Leprosy bacillus	Sodium salts of fatty acids of chaulmoogric oil. Ethyl esters of chaulmoogric and hydnocarpic acid	
Tubercle	Sanocrysin	Double thiosulphate of gold and sodium
Septic infections	Mercurochrome, etc.	

Ehrlich himself suggested that salvarsan should be tried in cases of anthrax, and in 1910 Eurich made the trial. Tests in vitro were carried out and gave presumptive evidence of the efficacy of the drug. Clinically it was found that the temperature might rise precipitately after the injection, but often fell critically in twenty-four or thirty-six hours; the œdema remained localized and quickly disappeared and the pustule dried and healed without suppuration. The mortality of malignant pustule treated by other methods is not very high, but certainly there seems some experimental and clinical support for the use of salvarsan in its treatment. For the septicæmic forms of anthrax salvarsan is useless.

The experiments of Morgenroth with optochin gave the first gleam of scientific hope that bacterial infections might be successfully combated by the intravenous injection of appropriate drugs. By the use of optochin Morgenroth was able to save 50% of mice suffering from pneumococcal infection, which is always fatal

to mice if untreated. But the use of the drug was abandoned in the case of human patients for two reasons: firstly, it sometimes caused blindness, and secondly, it did not cure the infection. The splendid work of Sir Almroth Wright on this subject is well known to us all, but not every experimenter has yet digested the sage comment which Sir Almroth makes in reference to animal experiment:—

"It is often forgotten that the conditions in the human organism may be fundamentally different from those in the animal, with respect to the form which the bacterial infection takes, the access of the blood fluids to the infecting microbes, the absorption and excretion of the drug, and the susceptibility of the nobler tissues to its toxic action."

This is sound clinical teaching.

In the treatment of leprosy remarkable results have followed the intravenous injection of the sodium salts and the ethyl esters of hydnocarpic and chaulmoogric acids. There is a consensus of clinical opinion as to their efficacy in greatly alleviating or curing the disease, but it is (so far as I am aware) not claimed that the drugs have any direct bactericidal effect. On clinical evidence, however, they should be classed as indirect germicides for the leprosy bacillus.

Everyone is familiar with the recent discussion as to the virtues of sanocrysin in cases of tuberculosis. I would not, even if I could, burden you with the evidence as to its merits, but content myself by giving the generally received opinion that sanocrysin has no direct—and a very doubtful indirect—germicidal action on the tubercle bacillus. Since the administration of the drug is not without danger, it appears to have a very restricted field for its use.

Coming finally to the drugs which have been used in severe septic infections, we find ourselves on very controversial ground. Great claims have been made as to the value of the intravenous injection of certain well-known antiseptics. Solutions of the hypochlorites, perchloride of mercury, mercurochrome, various aniline dyes and other drugs have been tried. What evidence have we that they either act as germicides or are of any indirect benefit?

No one who has followed the work of Professor Fleming on the action of antiseptics can continue to believe that any of the commonly used antiseptics could possibly exert a direct germicidal action on septic organisms in the blood-stream without at the same time poisoning the patient. Any effect which they may produce must be an indirect one and can only be judged by clinical results. Now these clinical results are very variable and unconvincing. The present position can be summarized by considering the views held as to mercurochrome. This drug will kill septic organisms in vitro in considerable dilutions and many observers have related series of dramatic cures obtained by injecting it intravenously. Hampton Young, of Baltimore, is a strong advocate for its use. But when one studies the series of cases which are published and notes the small series of conclusive and the large number of indeterminate results, and reflects that the writers were in some cases enthusiasts and sometimes used several other means of treatment also, and that control series were absent, there remains little but chance to account for the cures. I say "little but chance," because I believe there is sufficient evidence to show that in rare cases the disturbance induced by the injection of the drug must have been the main factor in bringing about recovery. But the action is so uncertain that the use of the drug must be accounted as very unscientific, and as a reckless shot in the dark. Certainly the routine intravenous use in septic infections has no justification.

The drugs which are more likely to be of benefit in septic infections are salvarsan and neosalvarsan. These drugs when injected intravenously certainly temporarily increase the bactericidal power of the blood, increase leucocytosis and, by diminishing the coagulability of the blood, may improve the circulation in congested parts.

Speaking as a clinician, I often feel the force of the criticisms aimed against us by those who say that we too readily adopt methods of treatment which are based

upon an insecure scientific foundation—in other words, we have too much of the quack within us. Anyone who cares to study the journals will find abundant evidence that both surgeons and physicians are too ready to try a remedy because it is new rather than because it has good credentials, and to believe that the presumed remedy has cured because cure has resulted. This fallacy is common in the case of the intravenous use of germicides.

On the other hand, as a clinician who has the highest respect for the bacteriological worker, one cannot be blind to the fact that the laboratory worker is often inclined to lay down hard-and-fast laws on experimental evidence which may at first seem perfect, but which may later be proved to include a fallacy. For this reason a closer co-operation between the two groups of workers is to be encouraged.

Professor Alexander Fleming: In any discussion such as this it is first of all necessary to know what we mean by the term "germicide." It is obvious that a germicide must be something which will kill microbes, and I have to thank my master, Sir Almroth Wright, for this definition: "A germicide is a substance which will enter into destructive combination with a microbe." I think we shall all agree that it would be wrong to class as germicides substances which in the concentrations employed do not kill microbes *per se*, but when injected into the circulation are reputed to undergo or induce some possibly mysterious change by which the antibacterial power of the blood is enhanced. Otherwise all manner of substances would have to be classed as germicides, for instance, nuclein, vaccines, and hypertonic salt solution. We may think that vaccines are potent agents with which to cope with infections, but this discussion is not one on vaccine therapy. It may seem to you ridiculous to mention these things, but at the last discussion on antiseptics which I attended, the surgeon who opened it dealt entirely with substances having about the same germicidal power as typhoid vaccine.

The definition of a germicide as a substance which will directly destroy microbes leaves us with a comparatively simple problem. We can estimate the germicidal power of any substance in blood outside the body by the simple method of adding it to infected blood, and after a lapse of time noting whether or not the bactericidal power of the blood is increased. In the body there are certain factors which may interfere with the action of any germicide which may be introduced, but it is absolutely inconceivable that any chemical will act as a direct germicide in the circulating blood when it fails in a like concentration to increase the bactericidal power of blood in a test tube.

For a germicide to be successful in killing bacteria in the circulating blood two essential conditions must be fulfilled. It may be that even if they are fulfilled, the practical result will be negligible, but if they are not, failure is inevitable. These conditions are: It must be possible *with safety* (1) to obtain a concentration of germicide in blood which is lethal to the microbes; (2) to maintain such a concentration sufficiently long for the microbes to be killed.

Another important point to be considered is whether the germicide acts only on one or two species of microbes or on many. The importance of this last condition is often lost sight of in practice, and we find an antiseptic which has been shown to have a powerful lethal effect on one microbe used to combat an infection with another to which it is relatively inert.

There are tests by which the bactericidal power of human blood can be estimated with a considerable degree of accuracy, and by using these tests any enhancement of this bactericidal power by the introduction of a germicide can be measured. In the literature regarding intravenous use of chemicals as antiseptics, there is, except in one or two instances, a singular lack of investigation as to the direct action of the chemical.

It is obvious that any germicidal substance which is introduced intravenously must be at its maximum concentration immediately after the injection, before it has had time to be removed from the circulating blood. It follows therefore that the blood taken immediately after the injection of a germicide, containing, as it does, the maximum concentration of such germicide, should show the maximum antibacterial effect, and if a series of samples of blood are taken at intervals after the injection, the antibacterial power of the blood should gradually fall as the germicide injected is excreted or removed from the circulating blood.

It seems quite clear that if immediately after a chemical is injected there is no increased bactericidal power in the blood, but that after a lapse of time the bactericidal power becomes greater, such an increase cannot be ascribed to the direct germicidal action of the chemical—in other words the chemical is not acting as a germicide and should not be so labelled. We will return to this later.

Normal bactericidal power of blood.—Before proceeding to any experiments with antiseptics in blood it is first necessary to understand what happens when we put microbes into blood. I will confine my attention to the ordinary pyogenic microbes, staphylococci, streptococci, *B. coli*, etc. Now all these are killed in large numbers by ordinary human blood. As an instance of this, if 1 c.c. of blood infected with from 2,000 to 5,000 staphylococci is incubated for 12 to 24 hours, some 90 per cent. of the cocci will be destroyed. Of course the actual number killed will vary with the virulence of the culture, the quality of the blood, and probably other factors. The active agents in the destruction of these pyogenic microbes are the leucocytes and if these are removed (as can be done by simple filtration through cotton wool) then the whole of the bactericidal power of the blood is lost and every one of the pyogenic microbes implanted will grow out.

Use of deleucocyted blood to determine the antibacterial power of chemicals.—The direct antibacterial power of any chemical in blood, therefore, can easily be tested by adding graduated quantities of the chemical to deleucocyted blood, and after incubation, noting in what concentration growth is inhibited. The deleucocyted blood has in itself no antibacterial power, so any inhibitory power must come from the chemical. This method rather flatters the chemical as in practically every instance the inhibitory power on the growth of the microbe is greater than the germicidal power.

Effect of adding chemicals to blood containing its full complement of leucocytes.—When a chemical is added to the blood containing its full complement of leucocytes the conditions are much less simple. Several things may be happening simultaneously :—

(1) The chemical may be killing the bacteria.
(2) „ leucocytes „ „ „ „ „
(3) „ chemicals „ „ „ „ leucocytes.

A simple experiment with carbolic acid will illustrate these points.

A series of dilutions of carbolic acid is made, and to one volume of each of these dilutions is added an equal volume of defibrinated blood infected with staphylococci (about 2,500 per c.c.). Equal volumes (50 c.mm.) of these mixtures are placed in slide cells and incubated. The result obtained is shown in fig. 1. Of the 56 microbes which were implanted into each slide cell only one grew in the control where the carbolic acid was replaced with salt solution. In the weakest dilutions of carbolic acid the result was the same. As the concentration of carbolic acid became stronger and stronger so the number of microbes developing increased until at a concentration 1 in 640 every staphylococcus implanted grew out into a colony. Here the whole of the bactericidal power of the blood had been lost and this was due to the carbolic acid having destroyed the leucocytes while it allowed the microbes to grow unhindered. As the concentration of carbolic acid was increased still further, the microbes were eventually inhibited and the antiseptic action of the chemical was manifest.

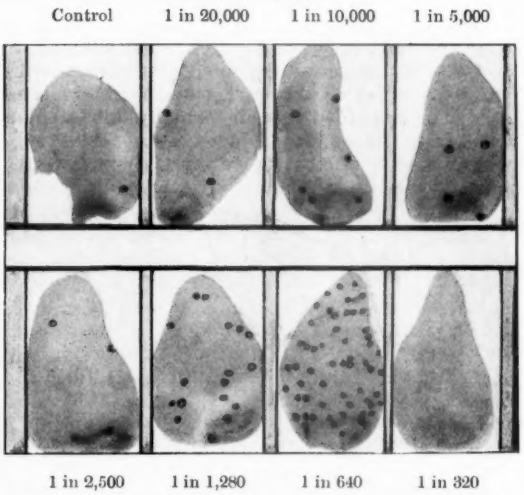

Fig. 1.—Carbolic acid. Effect on staphylococci in blood. Equal volumes (25 c.mm.) of infected blood and dilution of antiseptic.

25 c.mm. of blood plated on agar gave 56 colonies.

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There are therefore three zones of concentration of the antiseptic as regards its action on microbes in blood:—

(1) An *indifferent* zone where there is no action either on the bacteria or the leucocytes.

(2) An *antibactericidal* or *antileucocytic* zone where the leucocytes are damaged or destroyed and the bacteria are unaffected. A more copious growth of bacteria results.

(3) An *antiseptic* zone where the leucocytes are destroyed and the bacteria are killed or inhibited.

There is no suggestion that carbolic acid might be used as an intravenous germicide but this result is typical of almost all chemicals whether classed as germicides or not.

Let us now see how some of the germicides which have been recommended for intravenous injection fulfil the two requirements laid down.

Eusol.—This was originally recommended for intravenous injection in generalized infections following war wounds.

The dose suggested was 150 c.c. Taking the blood volume as 5 litres, this would mean that the maximum concentration of eusol in the circulating blood would be about 1 in 33.

Figure 2 illustrates what happens when eusol is incubated in slide cells with blood infected with hæmolytic streptococci. The control blood without eusol is able to kill all the streptococci. At a concentration of eusol 1 in 32 there is a distinct impairment of the bactericidal power shown by the growth of a number of streptococcus colonies and consequent hæmolysis of about one quarter of the blood in the cell. In concentrations of 1 in 16 and 1 in 8 the streptococci have grown freely and completely laked the blood. In a 1 in 4 dilution some sixteen colonies of streptococci have grown (although with this concentration even the red corpuscles are altered to a brown colour), and it is only when a concentration of 1 in 2 is reached that the streptococci are inhibited. To reach this concentration

5 litres of eusol would have to be injected into the veins and a consideration of fig. 2 will show that the 150 c.c. recommended can have no germicidal effect, although it has possibilities for harm.

CONCENTRATION OF EUSOL.

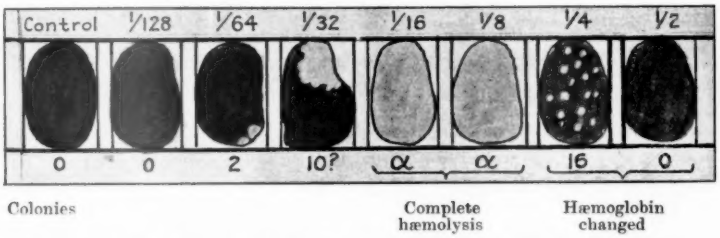

FIG. 2.—Effect of eusol on the growth of *Streptococcus pyogenes* in human blood.

CONCENTRATION OF MONSOL.

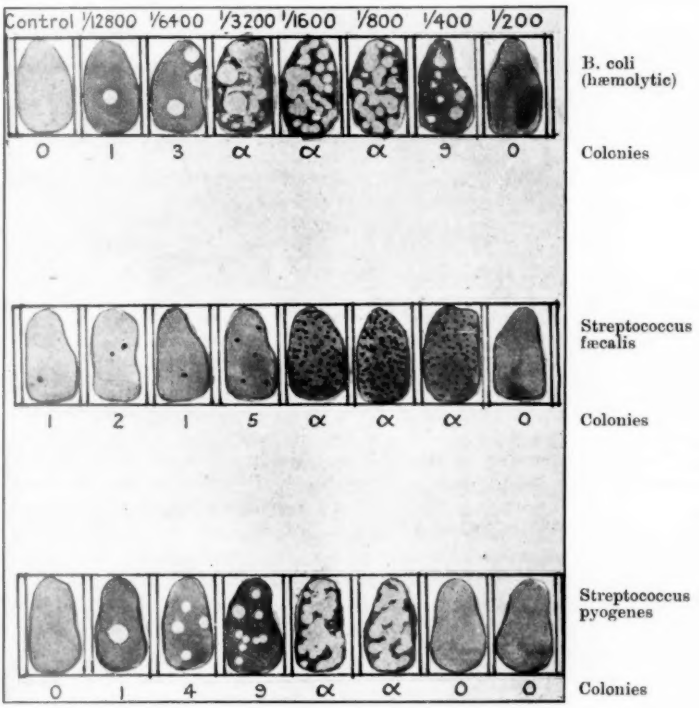

FIG. 3.—Antibacterial action of monsol in human blood.

Monsol.—This has been recommended for intravenous injection as a germicide. My findings with regard to the bactericidal action in monsol in blood are illustrated in fig. 3. The same zones are seen as were noted with carbolic acid. To reach an

antiseptic concentration, i.e., a concentration which will inhibit the bacterial growth in human blood would seem to require in the case of *B. coli* and *Streptococcus fæcalis* the intravenous injection of 2½ litres of a 1% monsol solution and in the case of *Streptococcus pyogenes* half this quantity. Lesser quantities, even if they were wholly retained in the circulation in an active state, would seem to be incapable of sterilizing the blood, although as can be seen from fig. 3, they might render it a better culture medium.

Quinine.—This has been much used in certain quarters as a germicide, especially suitable for intravenous injection in cases of puerperal fever due to the hæmolytic streptococcus.

Fig. 4 shows the bactericidal power of quinine hydrochloride on the hæmolytic streptococcus in deleucocyted blood and also the effect of the drug on the normal bactericidal power of blood. It is clear that the antiseptic concentration in the blood is 1 in 1,000 and that any concentration between 1 in 2,000 and 1 in

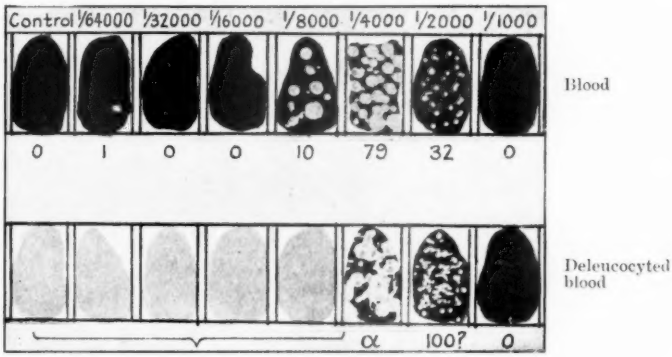

Fig. 4.—Bactericidal action of quinine on *Streptococcus pyogenes.*

8,000 renders normal human blood a better cultivation medium (by destroying the leucocytes).

To reach a concentration of 1 in 1,000 in blood would require the intravenous injection of at least 80 gr. of quinine hydrochloride, but fortunately the doses recommended (about 2 gr.) give only a concentration of about 1 in 40,000 which is well within the "indifferent" zone, and has no inhibitory action either on the bacteria or the leucocytes.

Mercuric chloride.—This is another drug which has had support as a germicide for intravenous injection in septicæmia, due to the hæmolytic streptococcus. When its bactericidal power was tested in deleucocyted human blood the following results were obtained :—

Test organism.	Concentration of mercuric chloride in deleucocyted blood.					
	1/4000	1/8000	1/10000	1/16000	1/20000	Control
B. coli	0	+	+	+	+	+
Staphylococcus	+	+	+	+	+	+
Streptococcus fæcalis ...	0	0	+	+	+	+
,, *viridans* ...	0	0	0	+	+	+
,, *hæmolyticus*	0	0	0	0	+	+

+ = growth. 0 = no growth.

The maximum effect is exercised on the hæmolytic streptococcus, but to reach an antiseptic concentration in the blood it would require something like $\frac{1}{3}$ grm. (= 5 gr.) The amount recommended is $\frac{1}{8}$ gr. The inference is obvious. Mercuric chloride in the doses recommended does not act as a direct germicide.

Mercurochrome.—This has in recent years had an enormous vogue as a germicide for intravenous injection. No specificity of action has been claimed and it has been recommended for infections by many microbes, among others staphylococcus, streptococcus and *B. coli*. The quantity used for intravenous injection is about 0·005 grm. per kilo body weight, which gives a maximum concentration in the blood-stream of about 1 in 15,000.

Let us now examine what happens when mercurochrome is mixed with infected blood in vitro. Defibrinated blood with and without leucocytes is infected with a suitable number of staphylococci, and 50 c.mm. of such infected blood is mixed with 5 c.mm. of mercurochrome solution and incubated in slide cells. The results are shown in Table I.

TABLE I.—EFFECT OF MERCUROCHROME ON THE GROWTH OF STAPHYLOCOCCI IN HUMAN BLOOD.

	Number of staphylococcus colonies developing in blood containing mercurochrome in concentration of			
	1/2000	1/4000	1/8000	Control (no mercurochrome)
Blood	20	18	8	1
Deleucocyted blood ...	74	84	93	89

The results with deleucocyted blood show that mercurochrome in a concentration of 1 in 2,000 has no power of preventing the growth of staphylococci in human blood, and the results with blood show that in these concentrations (which are fortunately not attainable in practice) the chemical, while having no antibacterial power itself, impairs the natural antistaphylococcal power of the blood.

In another experiment mercurochrome was added to deleucocyted human blood in a concentration of 1 in 6,000. This blood was infected with various microbes and incubated in slide cells. Controls were made, at the same time, of simple defibrinated blood (containing its full complement of leucocytes) and with similar blood containing 1 in 6,000 mercurochrome, both infected with the same number of microbes. The results are illustrated in fig. 5.

The microbes grow freely in deleucocyted blood containing mercurochrome, but very few were able to survive in blood alone without mercurochrome. It is a common belief that the antibacterial power of leucocytes is very small in comparison with that of a chemical "germicide." Here we have a direct comparison of the effect of mercurochrome and leucocytes on the growth of bacteria, and although the mercurochrome is in a concentration more than twice the maximum obtainable in an intravenous injection it has no germicidal action, whereas the leucocytes kill nearly all the microbes implanted.

The third column of cells where mercurochrome was added to blood containing its full complement of leucocytes will be discussed later (p. 58).

Sanocrysin.—This was introduced a few years ago with a great flare of trumpets as a remedy for tuberculosis. I was present at the meeting which inaugurated the campaign in England. We were told how in infinitesimal concentrations it killed the tubercle bacillus, how, when it was injected intravenously so many tubercle bacilli were killed that the patient was poisoned with his own dead bacilli and how, to combat this, a special antituberculous serum had to be injected. It seemed wonderful. We proceeded at once to test the efficacy of sanocrysin as a germicide to the tubercle bacillus in human blood. Sanocrysin in various dilutions was mixed with human blood infected with tubercle bacilli and the mixtures were incubated for some days after which the blood-clots were decolorized and stained. Fry has published the results obtained which showed that in the concentrations of sanocrysin

which could be obtained in the body and even in much higher concentrations the drug had no influence whatever on the growth of tubercle bacilli.

Now when sanocrysin is discussed in the treatment of tuberculosis, there is no mention of the wholesale slaughter of the bacilli by the direct action of the chemical.

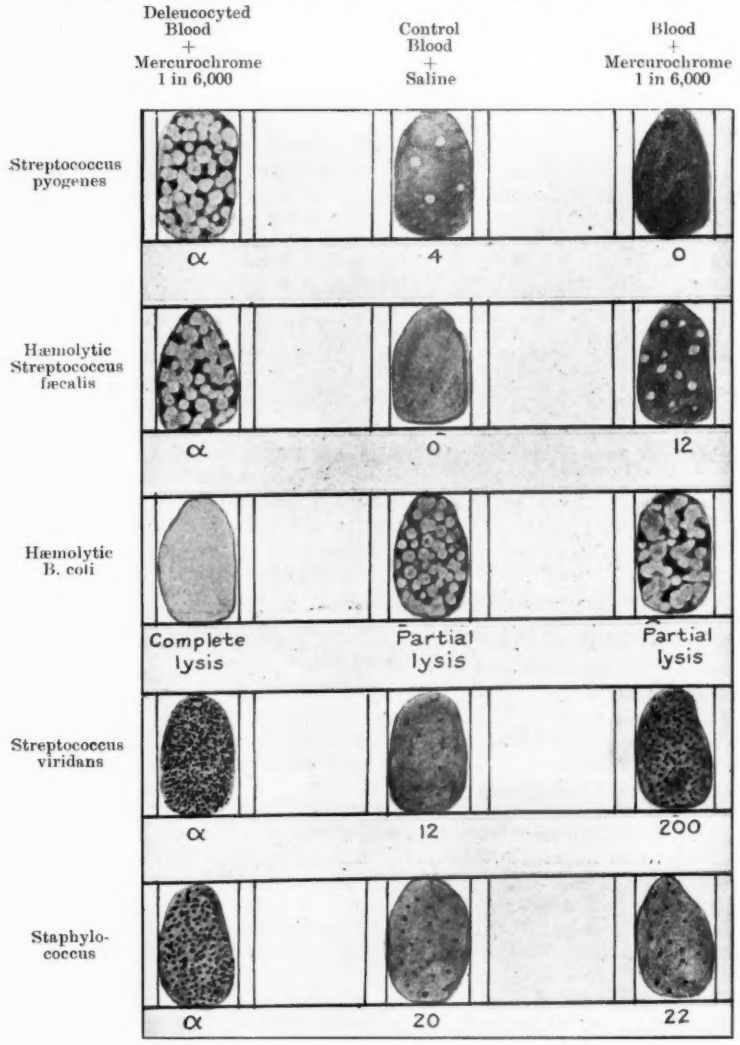

FIG. 5.

No antituberculous serum need be given to neutralize the poisons of the dead bacilli. Its reputed beneficial effect is attributed to some mysterious change which occurs in the body after its injection.

So far then the task has been simple. With none of the chemicals mentioned in the doses in which they are used can one obtain in the blood a concentration in which they are lethal to microbes. They have therefore failed in the first examination and cannot act as germicides in the circulating blood.

Aniline dyes.—Two of these have been especially recommended for intravenous injection as direct germicides—flavine and gentian violet.

Flavine.—This was recommended by Browning (1917) as an antiseptic which was very powerful on all microbes and which acted more strongly in serum than it did in a watery medium.

Flavine has a very slow lethal action on bacteria as can be shown by Table II. In the experiment represented by this Table a concentration of flavine of 1 in 20,000 was chosen, as an amount of flavine can be injected which when diluted in the blood can reach this concentration.

TABLE II.—RATE OF DESTRUCTION OF STAPHYLOCOCCI IN DELEUCOCYTED BLOOD CONTAINING FLAVINE IN A CONCENTRATION OF 1 IN 20,000.

Time of contact of cocci with flavine	Number of surviving cocci
At commencement	98·200 per c.c.
After 1½ hours	78·900 ,,
,, 2¾ ,, ...	51·200 ,,
,, 6 ,, ...	23·400 ,,
,, 24 ,, ...	13·700 ,,

The slowness of its action on bacteria becomes important when flavine is used for intravenous injection, as it makes it more difficult to fulfil the second condition that the lethal concentration must be maintained sufficiently long for the bacteria to be killed. This is rendered still more difficult by the affinity of flavine for the tissues. If an animal is killed immediately after a very large intravenous dose of flavine it will be found that all the tissues (except the central nervous system) are stained yellow, but the blood-serum has little or none of the flavine colour.

Information as to the direct germicidal effect of flavine injected intravenously can be obtained by taking blood before and at intervals after the injection and seeing whether the bactericidal power is enhanced. It is obvious that the dye must be at its maximum concentration in the blood immediately after the injection. And if blood taken then is incapable of inhibiting the growth of bacteria, then the flavine can have no direct bactericidal action.

Table III shows the effect of an intravenous injection of flavine on the bactericidal action of the blood.

TABLE III.

I.—*Rabbit* (20 c.c. flavine 1 in 1000)	No. of staphylococci developing	II.—*Man* (320 c.c. flavine 1 in 1000)	No. of staphylococci developing
Blood taken before injection ...	87	Blood taken before injection	24
,, ,, 1 minute after injection	62	,, ,, immediately after injection	94
,, ,, 3 minutes after injection	97		

It will be seen that the blood immediately after the intravenous injection of flavine grew staphylococci well. Although therefore it is possible to inject flavine sufficient, if diluted in the blood, to make a concentration lethal to microbes yet it disappears from the blood so rapidly that it is impossible to maintain such a concentration long enough for microbes to be killed.

Gentian violet.—This dye was shown by Churchman (1912) to have a very powerful inhibitory effect on the growth of certain bacteria, especially the Gram-positive microbes. It has with few exceptions comparatively little action on Gram-negative bacteria. The antibacterial effect is especially marked on staphylococci. It can be injected intravenously in such a quantity that if it were merely diluted by the circulating blood such blood would be definitely

bactericidal. Like flavine it is a slowly acting germicide, and like flavine it leaves the blood-stream very rapidly so that a minute or two after the injection the blood is no longer bactericidal. It would be impossible therefore to maintain in the circulation a bactericidal concentration for sufficient time to kill the microbes.

Arsenical preparations of the neosalvarsan type.—There is no doubt as to the efficacy of these preparations in certain spirochætal diseases. This we need not discuss. Douglas and Colebrook (1916) showed that salvarsan had a considerable bactericidal power on the hæmolytic streptococcus. Allison (1918) used it in the treatment of puerperal septicæmia. Colebrook (1928) has shown that the arsenical preparations have a very specific bactericidal action on hæmolytic streptococci. He has shown that novarsenobillon can be injected intravenously in such quantities that when diluted in the circulating blood a concentration lethal to the hæmolytic streptococcus can be reached. This drug then passes the first test.

In the concentration which is reached in the blood-stream it takes about six hours to effect the destruction of hæmolytic streptococci, and it has not been shown that with novarsênobillon it is possible to maintain a lethal concentration for this period. Colebrook, in fact, discarded intravenous injections of this substance for subcutaneous injections of metarsenobillon, and he has shown that by repeated injections, the blood-serum maintains its bactericidal action to hæmolytic streptococci for several days.

So far, then, the organic arsenical preparations are the only ones we have considered which can act as germicides in the circulating blood, and (apart from their spirochæticidal action) they act only on hæmolytic streptococci and the anthrax bacillus.

Specificity.—This is very well brought out by these arsenical preparations. They are very toxic to the hæmolytic streptococci, but are ineffective against other streptococci, so it is quite useless trying them in infections due to *Streptococcus viridans*. This specificity is well brought out in fig. 6.

Indirect Germicidal Action.

So far my comments have necessarily had to be, in the main, destructive. Let me now for a minute be constructive. For this purpose I must depart a little from the subject of the discussion. I wish to bring to your notice two methods of increasing the bactericidal power of the blood by the intravenous injection of chemicals.

(1) *A non-specific increase following the injection of substances definitely not germicidal.*—Common salt furnishes a good example. I have shown (1926) that when a hypertonic salt solution is injected into the blood the injection is followed by a marked rise in the bactericidal power.

With a small dose of hypertonic salt (say 50 c.c. of 10%) there is little or no preliminary drop in the bactericidal power of the blood, but with a large dose there may be seen a definite "negative phase" lasting for perhaps an hour, followed by a great increase in the bactericidal power lasting for some hours.

Table IV shows the sort of result obtained.

Table IV.—Effect of Intravenous Injection of Hypertonic Salt on the Bactericidal Power of the Blood.

	No. of colonies		No. of colonies
I.—*Rabbit* (3 c.c. of 10% NaCl)		II.—*Man* (50 c.c. 10% NaCl)	
Blood before injection ...	195	Blood before injection ...	135
,, 2 minutes after injection	250	,, 2 minutes after injection	145
,, 30 ,, ,, ,, ...	15	,, 1 hour ,, ,, ...	74
,, 2 hours ,, ,, ...	0	,, 3½ hours ,, ,, ...	0
,, 6 hours ,, ,, ...	0		

This change is not confined to salt but probably occurs to a greater or less extent after intravenous injections of all chemicals whether they are classed as germicides or not. The following figures were obtained after an intravenous injection of 320 c.c. flavine 1 in 1,000 into man.

	No. of colonies		No. of colonies
Blood before injection	24	Blood 30 minutes after injection ...	52
,, immediately after injection	94	,, 2½ hours after injection ...	2
,, 5 minutes after injection ...	67		

This increase in the bactericidal power of the blood 2½ hours after the injection cannot be due to the direct bactericidal action of the flavine which must then have

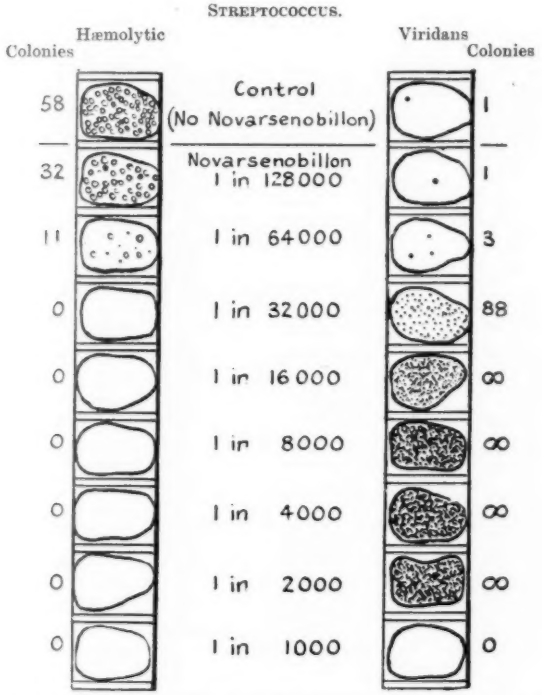

FIG. 6—Effect of novarsenobillon on the bactericidal power of blood on two different types of streptococci.

been in less concentration in the blood than immediately after the injection. Possibly the beneficial results which are said to have followed the intravenous injection of germicides are due to this non-specific rise in the bactericidal power, but if this is true then there is no justification for the injection of chemicals which are toxic when the change can be brought about better by common salt.

(2) *The specific action of mercury compounds on hæmolytic streptococci.*—Mercury salts are old established germicides but I have already demonstrated that in therapeutic doses they cannot have any direct germicidal action in the blood. I have shown that with mercuric chloride and mercurochrome the microbes grow well in deleucocyted blood containing more of the germicide than can be introduced

with safety. There is, however, an interesting phenomenon manifest when mercury compounds are added to infected blood containing its full complement of leucocytes. Fig. 7 illustrates the results obtained in slide cells when mercurialized blood is incubated with *Staphylococcus*, *Streptococcus fæcalis* and *Bacillus coli*. In each case growth occurs in quite high concentrations and in addition there is a zone of increased growth where the leucocytes have been destroyed. Mercuric chloride, therefore, as regards these microbes, offers no hope of success as an intravenous injection.

The case is different with hæmolytic streptococci. A typical result of the action

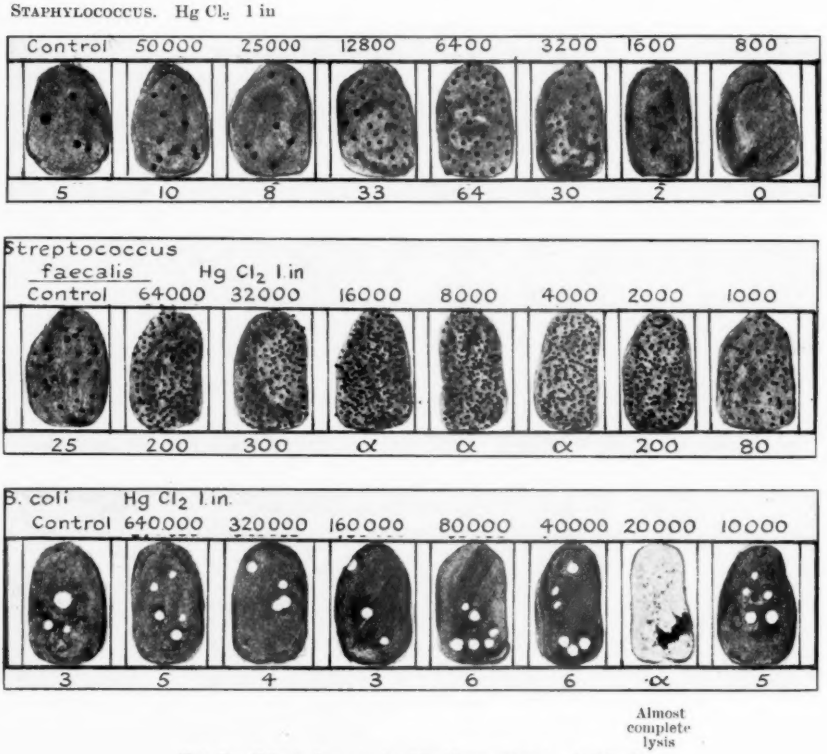

FIG. 7.—Effect of mercuric chloride on microbes in blood.

of mercuric chloride on the growth of hæmolytic streptococci in blood is shown in fig. 8.

Here there is no difference in the growth of streptococci in deleucocyted blood in any concentration of mercury from 1 in 20,000 downwards, showing that the mercury has no direct bactericidal effect in blood.

In blood with its full complement of leucocytes, however, it will be seen that there is a zone of greatly increased bactericidal power where the streptococci have been completely killed. In this particular experiment no growth occurred in blood containing 1 in 40,000, 1 in 80,000 and 1 in 160,000 of mercuric chloride. There was

good growth in concentrations of 1 in 320,000 and under, but at the other end of the scale it will be seen that a considerable number of colonies have developed in a concentration of 1 in 20,000.

In other experiments of a like nature with other strains of hæmolytic streptococci and other degrees of infection, it has been found that a distinct antibacterial effect may be manifest up to a 1 in 500,000 dilution of mercuric chloride.

We have already seen that the lethal agent on these streptococci cannot be mercury salt. The only difference between blood and deleucocyted blood is the presence of leucocytes in the former and it might be argued that the mercury salt combines with the leucocytes to form a bactericidal compound. This cannot be so, as in the 1 in 20,000 concentration of mercuric chloride which would be rich in this hypothetical bactericidal substance growth occurs.

It is significant that this concentration of mercuric chloride (1 in 20,000) is that at which the leucocytes are seriously damaged by the chemical as is shown by a consideration of fig. 7. It seems likely that growth results in this concentration

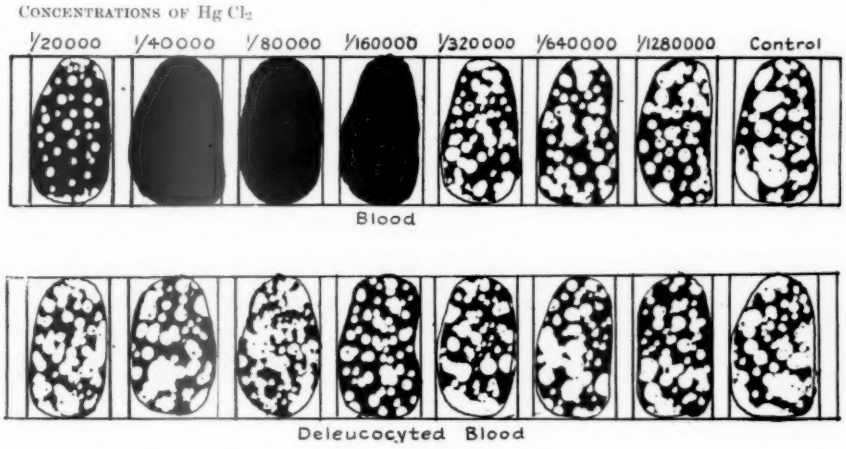

Fig. 8.

Action of mercuric chloride on hæmolytic streptococci in blood.

because the mercuric chloride cannot itself kill the streptococci and it damages the leucocytes to such an extent that they cannot function.

In the three cells which are sterilized the blood does not do the whole of the work, for in the control cell (without mercury) many streptococcal colonies have developed. It must, therefore, be a combined action of the mercury and the blood. The action of the mercury can hardly be a stimulating one on the leucocytes otherwise the increased bactericidal action would be manifest on all the microbes, whereas apparently it is only shown to the hæmolytic streptococcus. For the same reason it can hardly be an increase in the opsonic power of the serum. It would appear to be some action on the streptococci—not to kill them, but to make them more susceptible to leucocytic action. It can be shown that a concentration of 1 to 80,000 mercuric chloride has some inhibitory effect on the rate of multiplication of the streptococci for an hour or two, and it may be this retardation of growth which allows them to be destroyed by the leucocytes.

It may be, also, that the mercury neutralizes some toxic substance of the streptococci which is inimical to the leucocytes, but this is not so likely, as the

action can be seen equally with avirulent streptococci which are phagocyted plentifully in normal blood and with virulent streptococci which are much less readily picked up by the leucocytes.

This effect is seen, not only with mercuric chloride, but with other mercuric compounds. With mercuric iodide the following result was obtained:—

Hæmolytic streptococcus colonies developing in dilutions of mercuric iodide as under:—

	1/2000	4000	8000	16000	32000	64000	128000	256000	512000	Control
Blood	0	0	0	0	0	0	6	30	∝	∝
Deleucocyted blood	0	∝	∝	∝	∝	∝	∝	∝	∝	∝

Mercurochrome gave the following result:—

Dilutions of mercurochrome	20000	40000	80000	160000	320000	Control
Blood	0	1	10	16	∝	∝
Deleucocyted blood	∝	∝	∝	∝	∝	∝

Let us return to a consideration of fig. 5. Earlier in the discussion it has been pointed out that mercurochrome had no germicidal action *per se*, but that the leucocytes of human blood were capable of destroying nearly all the microbes implanted. When, however, the mercurochrome was added to blood containing its full complement of leucocytes (shown in the third column of cells) there was greater killing of hæmolytic streptococci than there was with the blood alone. With the other microbes, however, there was no improvement, indeed, there was more growth with the added mercurochrome, which is only to be expected, as in this concentration (1 in 6,000) the leucocytes are to some extent damaged (see Table I).

It is clear from these experiments that mercuric compounds have some specific action on hæmolytic streptococci, rendering them more susceptible to the normal antibacterial agencies of human blood. It is probable that some mercury compound will be elaborated which will be more potent than those cited, and it is possible that by the application of this principle—the use of a chemical not to kill bacteria but to act as an adjuvant to the natural defences—the most beneficial results will be obtained in that dreaded condition, a generalized *Streptococcus pyogenes* infection.

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Mr. P. H. Mitchiner said he had never met anyone who believed that one could get a direct germicidal action with any chemical in the blood. Chemical antiseptics given intra-venously must be given in such strength as to have the optimum lethal action on the micro-organism, without impairing the defensive action of the leucocytes or other tissue cells, and their maximum action must be at the moment of injection, so that even surgeons could not hope to obtain benefit from the injection of germicides. He was certain, from his experience, that in most cases the intravenous injection of so-called germicides was more harmful than beneficial to the patients who had septicæmia. Further, there seemed to be no criterion, in any particular case, as to what dose was likely to produce the most beneficial result especially as at different stages of the disease different doses were necessary in order to obtain the optimum effect. Test-tube experiments as to bactericidal effects were of no use when assessing their effects in the human body. A dose which was lethal to a micro-organism in the test-tube would permit the organism to grow in the blood. Like Professor Fleming, he proposed to deal only with bacteria, omitting the question of the protozoa. Though it had been advocated that the kind of drugs in

question should be injected for localized infections which showed a tendency to spread, such as cellulitis and carbuncle, no beneficial effects could be expected, since the localization of the trouble proved that the body defences themselves were capable of dealing with the infection. He would therefore consider only such results as he had seen in general infections.

In regard to chronic infections he was indebted to his colleagues in different departments at St. Thomas' Hospital for informing him of the results to which he would refer. He first went to the venereal disease department, because for generalized infections with syphilis, drugs had been used intravenously since Boticelli advocated the intravenous injection of perchloride of mercury, but with very disappointing results. Colonel Harrison told him (the speaker) that the intravenous injection of arsenic compounds was a satisfactory cure of syphilis, producing a definite disappearance of the spirochæte, but he did not claim that this was due to direct germicidal action. Further, when he (Mr. Mitchiner) looked into the figures, he did not think the results were perfect, as he found that it was customary for syphilitic patients, who had been treated with a full course of neosalvarsan, to return in a year's time, a large proportion having a positive Wassermann reaction, showing that the infection had manifested itself in the absence of the drug. In 50% of active tertiary lesions the Wassermann reaction was negative.

In the tuberculosis department he learned that Dr. Hebert had used sanocrysin in a series of 20 cases, and the results were quite negative, but it was now thought there to be of value in acute pneumonic cases in which recent spread had taken place.

With regard to acute generalized infections : he believed, from the clinical standpoint, that staphylococcal septicæmia was more fatal than the streptococcal form, and he had begun to separate the two forms, but, unfortunately, in many cases he could not do so, as the causative organism was not indicated. He found that various drugs had been given, including eusol, mercurochrome 220, and mercuric chloride, but in all cases there seemed to be a tendency to withhold these drugs until the patient was practically moribund, which appeared to show that most surgeons thought that these drugs were called only as a last desperate throw. Those who had much to do with septicæmia must have seen many cases, clinically regarded as hopeless, which had suddenly taken a turn for the better without any treatment. Therefore it was certainly courageous, if not foolhardy, to attribute to the injection of a small amount of chemical substance the cure of a case of septicæmia because an improvement took place immediately or shortly after the injection. It could not be proved, either one way or the other. He felt that in at least some of these cases the injection had had nothing to do with the cure of the patient. His clinical ignorance led him to attribute the increased germicidal power of the body tissues to protein shock. He thought that, as in the case of serum, if it did any good at all, it did so by altering the balance of resistance in the body tissues in some way.

If he were asked what were the clinical indications for the intravenous injection of these so-called germicides, he would say: (1) the failure of the patient to react to general anti-septicæmic treatment, such as the injection of saline; (2) the absence of leucocytosis, as seen in the blood-count. Professor Dudgeon had recently published in the *Lancet* a paper dealing with 200 cases of streptococcal and staphylococcal septicæmia, half of which he treated with perchloride of mercury, and half with mercurochrome 220. Out of the whole number there were forty-seven deaths. Professor Dudgeon frankly stated that he had had no success with these injections in malignant endocarditis, and that his best results were in puerperal septicæmias, of which, out of twenty-seven cases so treated—with perchloride—twenty-two recovered.

He (the speaker) therefore went to Mr. Wyatt, who had the care of the L.C.C. beds for puerperal septicæmia cases in London, and, through his kindness

and the hard work of Dr. Ingster, who had helped Mr. Wyatt for many years, he was able to secure a series of cases just as they entered the wards. The first was a series of five cases of septicæmia which had been treated neither with serum nor with perchloride. Four of the patients recovered, the fifth died. Fifteen cases were then tried with serum, and only four patients recovered; eleven died. There were then eleven cases treated with perchloride, one-sixteenth of a grain daily being given. Six of the patients recovered, five died. His own experience was that such cases did better without injection treatment than with it. He had looked up cases which he had had under his own care or supervision or immediate notice at St. Thomas's Hospital, i.e., cases of streptococcal septicæmia during the last few years. During 1925 he saw four cases of streptococcal septicæmia. One had injections of $\frac{1}{16}$ gr. of perchloride of mercury on three consecutive days, and the patient died on the third day. The other three cases had no germicide treatment; two patients died, one recovered. In 1926 he had seven cases of septicæmia, one of them staphylococcal. As mercurochrome was being used a good deal in that year, three of these patients were treated with it: two died, one recovered. Of the four cases which had no such treatment, three died, one recovered. In 1927 he had one case, which was fatal; it was a staphylococcal case, and the patient was moribund on admission to the hospital. In 1928 there were four cases, two of which were treated with perchloride and they both recovered; the two which were not so treated died. In 1929 there were four cases of streptococcal septicæmia. Two patients were treated with perchloride, and both died; two were not treated with any such drug: one died, one recovered. In 1930 there were four cases of streptococcal septicæmia; two were treated with perchloride and both patients died; of the others, one recovered, one died.

It would be agreed, therefore, that the value of this treatment was, to put it mildly, very doubtful.

Mr. T. H. C. Benians said that a nurse probationer answering a question on the use of disinfectants had said: "Disinfectants are nasty dangerous things; they kill bacteria and human beings." He was reminded of that answer as he listened to Professor Fleming, except that he now gathered that they did not kill bacteria. He asked for some leniency, or, in fact, accuracy, in defining the term germicides, which, in his opinion, might act either directly or indirectly. He reminded Professor Fleming that the "blow direct" was all very well, but the body did not go in for those blows, and whilst he had been very much impressed by Professor Fleming's demonstration, he thought that one had to be extremely careful about translating experiments in vitro into results in vivo. The time would come when a different interpretation of these experiments would obtain.

Taking a philosophic survey of disinfectants in general, we found that, now we had learnt their lesson, they were being displaced from all their original spheres of use; almost the only place where the success of germicides was maintained at the present time was actually in the blood-stream. He referred of course to protozoal infection, but between these successes and the failures in the treatment of bacterial septicæmias there was a big gap. Something had already been done in bridging that gap and he proposed to consider certain experiments in which bactericidal sera had been produced, to show how they failed when they came to clinical application.

Morgenroth's "optochin" was unquestionably a success; it was absorbed and no doubt circulated through the blood and cured cases of generalized pneumococcal infection in mice, a very severe test. When tried in the treatment of human pneumonia, however, it failed. Pneumonia should be regarded as a massive abscess in a single organ and this would not be permeated by disinfectants put into the blood-stream. Browning showed that euflavine could produce a germicidal serum, although he never claimed to cure infection with it. Tubby, Mackie and others,

applying it to generalized staphylococcal infections in rabbits, found it a failure. Those who had worked on staphylococcal septicæmia in rabbits knew that multiple abscesses in the kidneys were a characteristic feature, and these, he thought, caused the death of the animal. Then there was Colebrook's work with the arsenobenzols. Colebrook had shown that there was a bactericidal power in the serum with regard to hæmolytic streptococci, and that it could be maintained. He had also shown a method of assessing the damage done to the phagocytic tissues of the body. Colebrook tested that by the action of the drugs on the leucocytes of the blood-stream, and this he (the speaker) regarded as an unsatisfactory test. The leucocytes were, in many ways, some of the least permeable cells in the body, and if they were used as a basis for judging what damage was done to phagocytic tissues in general, the conclusions arrived at might fall far short of the mark.

The trouble in all these instances appeared to have consisted in the mechanical conditions in the body rather than in the lack of germicidal power of the blood, and we should not turn back at this point and say that intravenous germicides were an impossibility. With regard to the clinical use of germicides: at one end of the scale of septicæmia infection there was the acutely toxic type, at the other end there was the true pyæmia, in which occurred thrombosis and embolism. In a case of the latter the patient did not die from bacterial toxæmia so much as from the accidental formation of abscesses in dangerous situations, such as the joints, pleura, pericardium, or even heart muscle.

Taking first the toxic type of condition with little in the way of abscess formation, supposing one were able to kill all the bacteria in situ, theoretically at any rate one liberated all the toxins at once, and they would attach themselves to important tissues, especially the nerve tissues, and so the degree of toxæmia would be very much increased. Professor Fleming had a great belief in the power of the leucocytes, but although the organisms in these infections were deadly, the leucocytes would not touch them. If an organism got into the body it must either be lysed in the blood-stream, or taken up by phagocytes and digested. If it were digested, it would probably be changed into a form which would do the body little damage afterwards. If the bacterial substance was lysed in the blood, toxæmia was produced. In toxic cases we wanted the phagocytic activity, but failed to get it. We must try to introduce detoxicating agents. We were at present limited to the use of serum—and some streptococcal sera were moderately effective—or to immuno-transfusion, for this purpose, but he felt that germicides in such cases might do more harm than good.

In pyæmias with thrombosis, on the other hand, germicides could not kill the bacteria because they were mainly hidden in abscesses; thrombi were forming in vessels and leucocytic enzymes were breaking them down, so that infected emboli were scattered through the body. Some time ago, at a meeeting of the Section of Pathology, he had raised the question whether one should not try to reduce the number of leucocytes in pyæmic conditions; he thought that would have to be done if germicides were to be successful in these cases. He had tried the effect of benzol by mouth for this purpose in some cases of osteomyelitis; he believed with some success. The leucocyte could do much harm, and when performing autopsies on these cases one saw masses of leucocytes everywhere.

In conclusion he felt that the value of intravenous germicides would have to be determined by careful clinical use, since experimental work might show one thing and clinical experience something quite different. Arrangements should be made for the use of approved germicides, and these drugs should have issued with them a form for giving clinical and pathological, and where necessary, post-mortem data relating to the treatment and course of the case. The Medical Research Council or some other body should pay a fee to have these forms completed by the doctors using the preparations. This would give us a mass of clinical material, and would supersede the state of things now existing in which occasional successes were reported. Analysis

of the data by some authoritative committee could then be undertaken and some useful results would be available.

Dr. L. P. Garrod said that he had recently done some work to determine in what concentrations five germicides, some of which had been mentioned this evening, could kill or inhibit the growth of *Streptococcus pyogenes* in the presence of blood.

Eusol was included because it had been given intravenously, but it had no action whatever under these conditions. Of the remaining four, none, having regard to the concentration attainable in the blood by intravenous injection, was calculated to exert a bactericidal action, and only one, acriflavine, appeared likely to exert even an inhibitory action. He had looked into the literature concerning mercurochrome, to see whether he could ascertain how the drug came to be looked upon as so effective a germicide, and he believed he had discovered the reason. The inventors of the drug, Young, White, and Swartz, in introducing it, stated that a 1-in-10,000 solution would kill *Staphylococcus aureus* in 15 minutes. Four investigators besides himself (the speaker) had found solutions varying in strength between 1 in 50 and 1 in 400 ineffective for this organism.

After hearing Professor Fleming's earlier remarks he had reflected that no one present would ever use mercurochrome again. But Professor Fleming had gone on to suggest that there was possibly a mysterious effect which it might exert other than a direct bactericidal one. The inventors, however, did not make such a claim; they said it was a powerful germicide, which would act as such in the blood. He, Dr. Garrod, maintained that subsequent workers had proved mercurochrome to be a very weak germicide. The difference between these results and Young's was explained by the fact that Young's dilutions were made in acid urine, and it had been proved that mercurochrome was a more active germicide in acid than in neutral solution. He suggested as a possible explanation of this that mercurochrome was decomposed by acids and that the killing action was due to a salt of mercury so liberated. He (the speaker) submitted that there was no evidence of mercurochrome being a sufficiently active germicide for use, at all events in the blood-stream.

Dr. G. M. Findlay said that on examining the chemo-therapeutic treatment of infectious diseases one found that the more highly differentiated the parasite, the more easily was it got rid of in the body. Bilharzia worms were readily killed by antimony salts, protozoal diseases were fairly easily eradicated, but bacterial diseases were scarcely affected by chemo-therapeutic agents, and diseases due to ultra-microscopic viruses were entirely unaffected by them. In protozoal diseases there was little evidence that the drugs which affected them had any direct influence on the protozoa, except in the case of amœbic dysentery. In kala-azar, pentavalent antimony compounds in vitro had no action, yet they were efficient in vivo. If an early case of kala-azar was treated by pentavalent antimony compounds these drugs were comparatively inefficient, and it was usual, in such cases, to allow them to go on for some weeks before antimony was given. The latter acted in association with the immune bodies formed in these cases. In malaria Colonel James had shown something of the same kind. When malaria was used for treating general paralysis of the insane, it was found that if quinine was given during the first attack of fever, the parasites were not eradicated, but if the patient was allowed to go on and have a fairly prolonged attack of fever, the parasites disappeared as a result of the quinine. It was known that the antitoxin content of the blood might be raised by the injection into it of non-specific substances, such as manganese, which had no direct action on the bacteria, and it was possible that, eventually, chemo-therapeutic drugs would be found which might stimulate the formation of immune bodies in bacterial diseases, and so lead to their eradication, not by direct action on the bacteria, but by acting in unison with the naturally-formed immune bodies in the tissues.

Dr. J. Burnford said that he had been pleased by Dr. Benians' reminder that where there was a focus of infection, it was not for the pathologist to interfere and try to eradicate that infection. The great flaw in this experimental work was that the problem was tackled as if there had been put into the blood-stream a certain quantity of streptococci or other organisms, and one was dealing with that quantity alone, disregarding the fact that there might be a storehouse of infection somewhere else in the body, which came within the province of the surgeon. That perhaps explained why the septicæmic and the pyæmic states mentioned by Dr. Benians did not respond to germicidal agents.

He had been impressed by the first two cases of staphylococcic pyæmia which he had treated with perchloride of mercury, and which had been cured, but subsequent cases had not impressed him. He had not met with a single cure of infective endocarditis by this or any other means. From the anatomical point of view, the cure of infective endocarditis was impossible; for how could one deal with the damaged endocardium and the growing vegetations? When the offending streptococcus came from the patient's intestine, it seemed hopeless to seek a germicide which would eradicate not only the circulating organisms, but also the original site of infection.

One interesting observation he had made was worthy of record. Blood-cultures previously positive in several cases of pyæmia had been negative 24 hours after intravenous injection of $\frac{1}{16}$ gr. perchloride of mercury in several cases of pyæmia and in one case of infective endocarditis. He would not attempt to calculate the extreme dilution of the perchloride in the blood-stream.

In other medical conditions, however, he had obtained satisfactory results from the use of so-called germicides. With perchloride of mercury he had had excellent results in influenza and influenzal pneumonia, though some might argue that equally good effects had been obtained where no germicide was used at all. With intravenous salicylates, particularly the drug tylcalcin, he was convinced that there were immediate results in rheumatic infections. So also with various other drugs he had used there was considerable empirical evidence that they produced an effect. He agreed, however, that the results could hardly be explained by direct germicidal action. In several cases gingivitis and even colitis with blood and mucus occurred after three or four injections of $\frac{1}{16}$ gr. of perchloride.

He still thought that in such a discussion as this one wanted experiences rather than results of laboratory experiments. One should not be biassed or turned aside by the pleasant cynicisms of Professor Fleming, or be too much influenced by the behaviour of his performing leucocytes. As experiments they were of interest, but could not be taken as indicative of the physiological processes at work in the living body. Nor were the polymorphic leucocytes the only cells concerned; the lymphocytes which manifested so much activity in certain infections had been sadly neglected by the experimentalists. Yet he agreed that some scepticism was necessary, and one must not be carried away by success in first treatments. There was still hope that chemotherapy would avail in certain infections.

Professor Fleming (in reply) said that much stress had been laid in the discussion on the value of clinical experiment in estimating the power of a germicide. Clinical experiment alone could only be useless in estimating the germicidal value of a substance, although, of course, no one would dispute its importance in the estimation of the therapeutic value of any chemical in any particular infection. The germicidal value and the therapeutic value were two very different things.

Mr. Zachary Cope (in reply) said that Ehrlich was the first to enunciate the principle that a germicide acted by entering into destructive combination with a microbe. That principle was generally accepted as true, but it would be a pity to let our respect for such a great authority close our minds to the possibility that microbes

could be killed in other ways. It was surely possible that a substance might act as a germicide without actually touching the germ. A minute fraction of difference in the pH of the surrounding medium might alter the environment unfavourably towards the microbe, and germicides might act by unfavourably affecting the conditions under which microbes lived. Because the medical man did not know, he should not decline to believe that these things were possible, otherwise he might fail to observe opportunities of advancing our knowledge. It was of interest to recall Kolmer's statement that,

> "our present knowledge of the specific treatment of protozoal diseases of man and the lower animals, and of trypanosomes and the spirochæte is almost confined to clinical experience with certain drugs rather than systematic chemotherapeutic investigation."

Millions of people had been saved by drugs for which laboratory sanction only followed long after their clinical value had been discovered. The treatment of protozoal diseases could not be excluded from any discussion of germicides.

Professor Fleming had revealed so many interesting things in the course of the debate that he (Mr. Cope) felt more hopeful than he had done when he had arrived at the meeting. He could not agree, however, that the maximal germicidal effect of a drug injected intravenously should necessarily be manifest in the first few minutes after injection, for it was quite possible that the microbe might be more sensitive to a dilute drug over a long period than to a stronger solution for a short time. Dobell and others, in their work on the germicidal effect of emetine on the *Entamœba histolytica*, found that it needed four days for a dilution of one in five millions to kill all the amœbæ.

It was interesting to see that in Professor Fleming's opinion the injection of mercurochrome in certain dilutions had a beneficial effect, even though it might not be termed a direct germicidal effect. Very helpful also was the evidence brought forward that the intravenous injection of strong salt solution tended to get rid of septic organisms in the blood. In cases of acute ileus with toxæmia the intravenous injection of 20% salt solution might revive the patient in a wonderful manner, and it was possible that there was some relation between the two facts.